VOLUME 12
NUMBER 8
AUGUST, 1959

ORAL SURGERY
ORAL MEDICINE
and ORAL PATHOLOGY

EDITORIAL

THE INTERNATIONAL ACADEMY OF ORAL PATHOLOGY

IN THIS day of international stress—idealogic, racial, and commercial—there is between men of all nations and philosophies one strong bond: the bond of science, particularly medical and dental science. In the hope of strengthening this bond, even in a small way, the International Academy of Oral Pathology became a reality on Jan. 29, 1959.

This activity is dedicated to the exchange of thoughts, concepts, and experiences in the area of oral pathology. To this end it will sponsor periodic conferences in various countries of the world and, in time, publish the transactions of these sessions. It is gratifying to know that the Charles Ulrick and Josephine Bay Foundation is generously supporting the Academy in its efforts to bring about a better understanding of oral disease. Dr. Lester R. Cahn and Colonel Joseph L. Bernier, founders of the Academy, have enlisted the advice and assistance of Professor Martin Rushton, Dr. Reidar Sognnaes, Dr. Kurt H. Thoma, Professor Robert Bradlaw, and Dr. Jens Pindborg in the planning of the Academy's activities. This group will constitute a board of trustees, with Dr. Lester R. Cahn as chancellor and Colonel Joseph L. Bernier as secretary-treasurer. The secretariat will be at the Armed Forces Institute of Pathology in Washington, D. C., Drs. Harold Hillenbrand and Henry A. Swanson will act as consulting associates.

The first conference will be held on Sept. 15, 1959, at the New York Academy of Medicine in conjunction with the centennial meeting of the American Dental Association. Because of the nature and format of the session, attendance will be by invitation.

It is of great significance that such an important activity in dentistry is supported by private funds. This is not another society of men banded together to espouse the political objectives of a specialty area; rather, it is a group of men acting on behalf of benefactors for the purpose of assembling scientists from all over the world to discuss their work in oral pathology. Conferences will be held periodically in a world city most convenient to the majority attending.

We are happy to extend our heartiest congratulations and best wishes to the International Academy of Oral Pathology which, beyond doubt, will play a most important role in uniting scientists throughout the world in an effort better to understand some of the ills of man.

K. H. T.

OPERATIVE ORAL SURGERY

INSTRUCTIVE CLINICAL CASE REPORTS

Part II

Theodor Blum, D.D.S., M.D., New York, N. Y.

For many years it was my privilege to give oral surgery clinics for the profession in hospitals and later, since 1927, in my office until I noticed that most of the observers were interested only in surgical procedures. The study of the patient, including history, x-ray findings, pulp testing, etc., was of minor interest, and clinical oral pathology was entirely neglected. This was one of the reasons for the founding of the New York Institute of Clinical Oral Pathology. Since 1933 monthly conferences have been held by the Institute, and study courses have been given twice a month from October through May. In the early years the monthly meetings, which were open to students, members of the Institute, and all dental residents and interns, consisted mostly of lectures; very few clinical pathologic conferences were included. The demand for conferences increased to such an extent that at present only two, or at the most three, lectures are given by very prominent educators. All this is mentioned to explain why my lectures stress case reports, which in my opinion are most instructive and provoke very lively, interesting, and fruitful discussions and study.

The question of removal or retention of third molars, particularly in the mandible, is still widely misunderstood. Therefore, I have chosen as my first case one which illustrates this problem.

Case 1.—An 18-year-old boy was referred for consultation with regard to his four third molars. Four extraoral films (Fig. 1) were submitted by the dentist. Clinical examination revealed that all third molars were unerupted and that the mandibular incisors were crowded. To bring the x-ray study up to date, additional extraoral and intraoral (regular bitewing and occlusal) films were taken (Fig. 2). In the x-ray pictures taken on June 16, 1955, aside from the slightly different angle from which they were taken, both mandibular third molars are seen in practically the same position. The left one is covered by more alveolus, which perhaps is a factor in its tight impaction against the second molar, while the corresponding tooth on the right is in normal eruption, as can be seen on the films taken

Presented before the New York University College of Dentistry Alumni Association on April 15, 1958.

two and one-half years later (Dec. 17, 1957). My films taken about one year later (Jan. 27, 1958) picture the left tooth in about the same position and the right one somewhat further advanced in its course of eruption.

To be fully prepared for diagnosis and treatment, roentgenograms had been procured as described above. I must repeat here the necessity of getting all possible information from such a study—a most important guide to the operative procedure if such is indicated. It must be admitted that correct predictions are not always possible, for which reason such patients must be studied at short intervals of three to six months. Too many third molars are sacrificed and others are permitted to remain in the jaws too long, resulting in a difficult operation. In previous papers further details have been discussed.

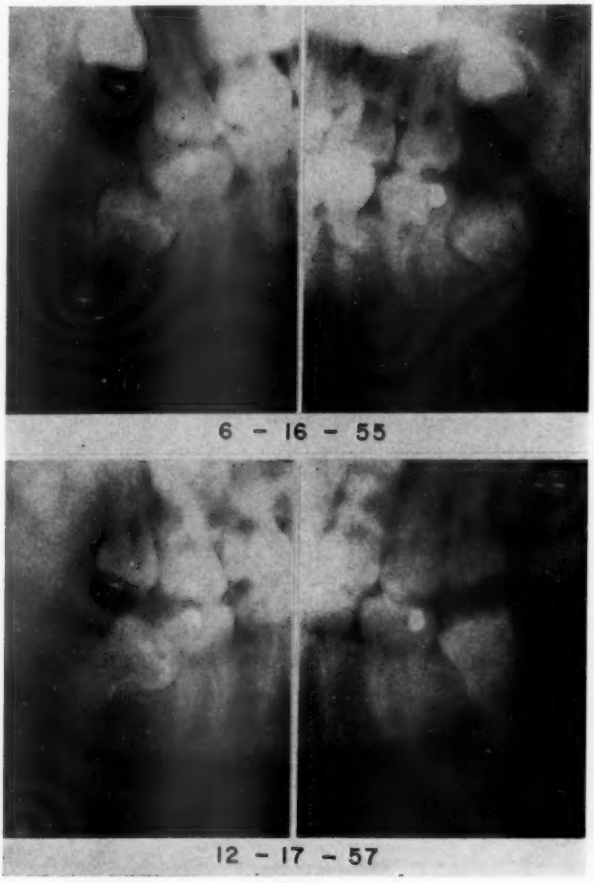


Fig. 1.

Here is a case in which, had films been taken in 1956 or a little later, not only could the definite tendency to impaction of the left mandibular third molar have been predicted but the tooth could have been removed before the roots were fully developed.

CASE 2.—A 38-year-old man came under my care on May 7, 1957. About three years earlier an oral surgeon had removed an impacted right mandibular third molar under local anesthesia. The wound did not heal properly and was treated for two to three months. A dentist also took care of the wound from time to time, assuming that there was periodontal

Fig. 2.

involvement of the distal root of the second molar. After a while the wound healed. However, it swelled periodically and subsided again. The area swelled about two months prior to my seeing the patient; antibiotics were given and the trouble cleared up, only to return four or five weeks later.

Clinical examination on the first visit was negative. Five films taken before and since the operation were submitted and studied (Fig. 3). My interpretation of the preoperative exposures was that the pericoronal area between the second and third molars was infected, for the bone border appeared irregular and apparently extended to and involved the apical region of the distal root of the second molar. In the next few films there was bone regeneration and even less involvement of the distal root. The last film again revealed loss of alveolus.

My films taken on May 7, 1957 (Fig. 4) are most instructive, each contributing its part in giving the correct findings. The extraoral view shows a clear survey, which includes the fact that there is loss of bone posterior to the second molar. This is also well seen on the bitewing exposure but obscured on the regular intraoral (periapical) one; the latter, however, gives a clearer idea of the periapical condition. The bitewing film also depicts a line of chronic productive periostitis—a strip of bone formation about 1 cm. posterior to the second molar.

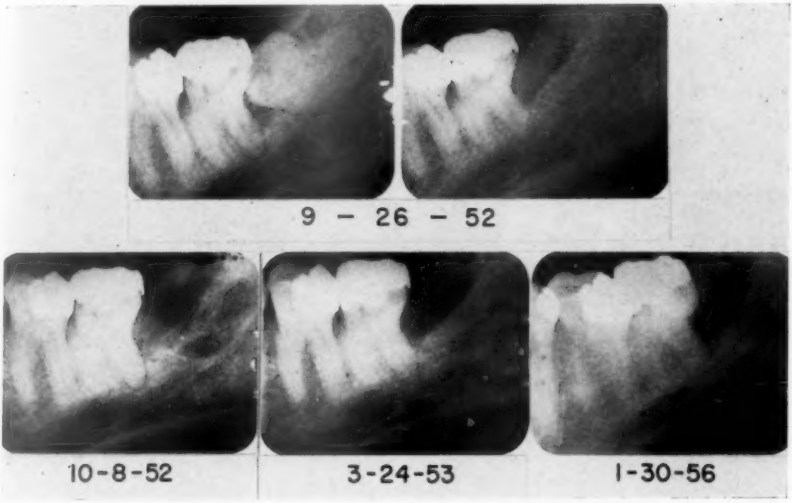


Fig. 3.

Since the condition was quiescent at this time and seemed to be improving, I suggested that the dentist's treatment be continued.

The patient returned on Feb. 4, 1958 (Fig. 4), having had quite a flare-up in the same area. It had started with sensitiveness in the second molar when he bit on that tooth. Submaxillary lymph nodes had become involved. The patient had used hot salt water mouthwashes and had taken some antibiotics, and the swelling had subsided. Although it was better, he thought that something could still be seen and came in.

My clinical examination revealed no discharge, but the soft tissue in the region of the second and third molars was slightly reddened. On the buccal side and distally, a probe could be inserted easily for about 1 cm. On Feb. 18, 1958, the pulp test response of the second molar was normal.

With these findings, I decided to remove the second molar and the diseased soft tissues. This was done under mandibular block anesthesia, and the specimen was sent to the laboratory for histologic examination. The diagnosis by Dr. Margit Freund, pathologist of The New York Institute of Clinical Oral Pathology, was as follows: "Viable pulp showing reticular

atrophy within the pulp chamber and chronic pulpitis in the apical third of the distal root. The pulp in the anterior root is normal. Denticles. Marked hypercementosis of the distal root. Deep pyorrheal pocket of the distal root. Periodontitis of the interradicular aspect of the distal root."

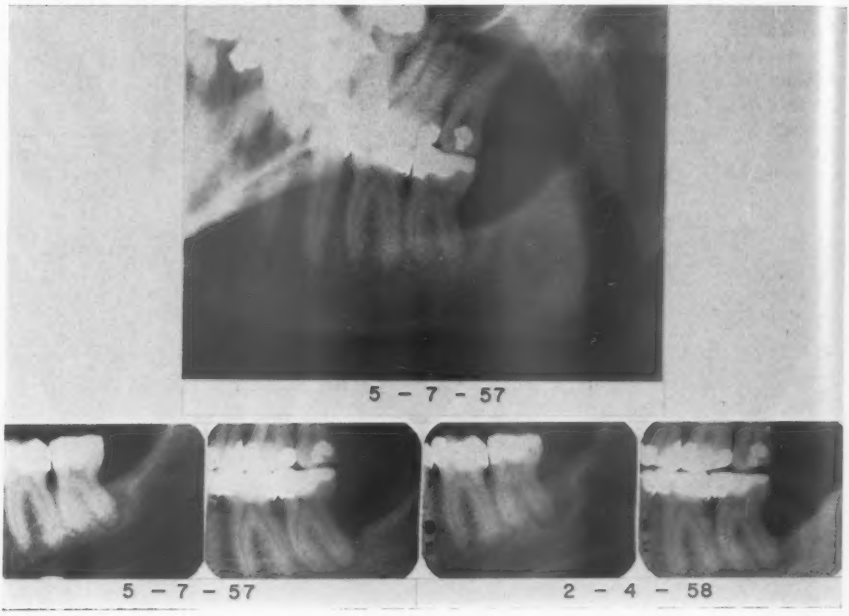


Fig. 4.

A critical view of the foregoing case is most difficult. If the final outcome could have been foreseen, the two molars would have been removed at the time of the first operation. With so much loss of alveolus at the posterior surface of the distal root at this time, root canal therapy for a patient about 35 years of age is not very promising. In this instance such therapy was beyond the patient's means, particularly, since success was doubtful. Under the circumstances, I am in favor of the conservative approach attempted here.

CASE 3.—A woman, 59 years of age, was referred by a periodontist. She had no complaint. The specialist found some pus exuding at the free gingiva around the right maxillary central incisor.

Examination disclosed a circular enlargement, nearly 1 cm. in diameter, on the labial side of this tooth. It was covered with normal mucous membrane, and at its highest point it was raised about 1 mm. Fluctuation could not be elicited.

X-ray examination showed an area of bone loss, nearly 1 cm. in diameter, at the middle of the root, beginning at the midline and extending over half of the root (Fig. 5, June 10, 1957). This can also be seen on the occlusal film, which was taken with the possibility of a nasopalatine cyst in mind. A pyorrheal pocket or pulp involvement had to be considered also.

The following operation was performed under local anesthesia: The incision (with Bard-Parker knife) was carried from the apical region of the left lateral incisor to the right one. The mucoperiosteal flap so outlined was elevated and held retracted. The involved area showed loss of bone on the labial side. The soft tissue filling the bone cavity was peeled out without much difficulty; a smooth, round, bony wall was exposed, and parts of the mesial,

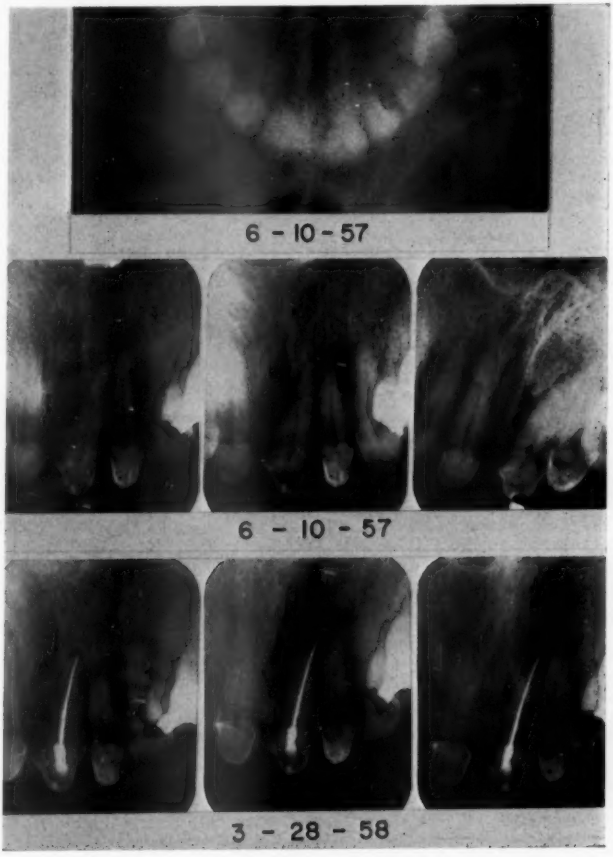


Fig. 5.

palatal, and labial sides of the root of the right central incisor were found denuded. The bony edges of this circular labial opening were cut away and smoothed off. No accessory root canal opening or connection with the nasopalatine canal was seen. All debris was removed, sulfanilamide powder was placed all over the wound and under the periosteum, and the flap was replaced and held in position with three catgut sutures. The closed wound was covered with iodoform gauze and sulfanilamide powder, which were to remain in position until the patient returned the next day. The specimen was sent to the laboratory, and the following diagnosis by Dr. Freund of the New York Institute of Clinical Oral Pathology was reported: "Epithelium containing granuloma with cyst formation." This report verified the suspicion that the lesion was caused by an infected pulp through an accessory canal and foramen. Therefore, root canal therapy was instituted.

Careful study of the roentgenograms taken after root canal therapy reveals the filling material entering the accessory canal (Fig. 5, March 28, 1958).

In reviewing this case, I must admit that the area of bone destruction, as seen in the original films (taken on June 10, 1957), is very much unlike a pyorrheal pocket and that the location is not typical of a nasopalatine cyst.

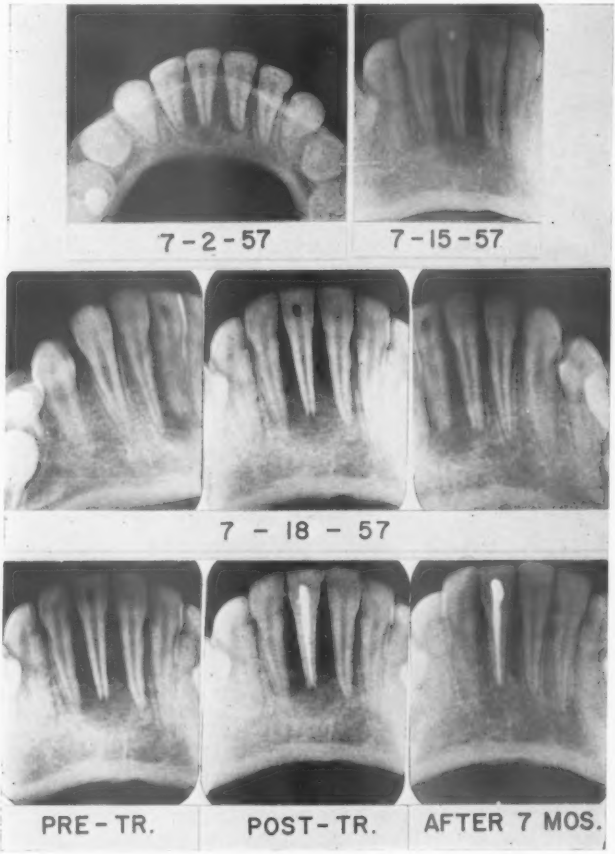


Fig. 6.

The porcelain jacket on this tooth made it impossible to use the pulp tester, which would have verified one of the tentative diagnoses. When the pulp chamber was entered, however, the pulp was found to be necrotic.

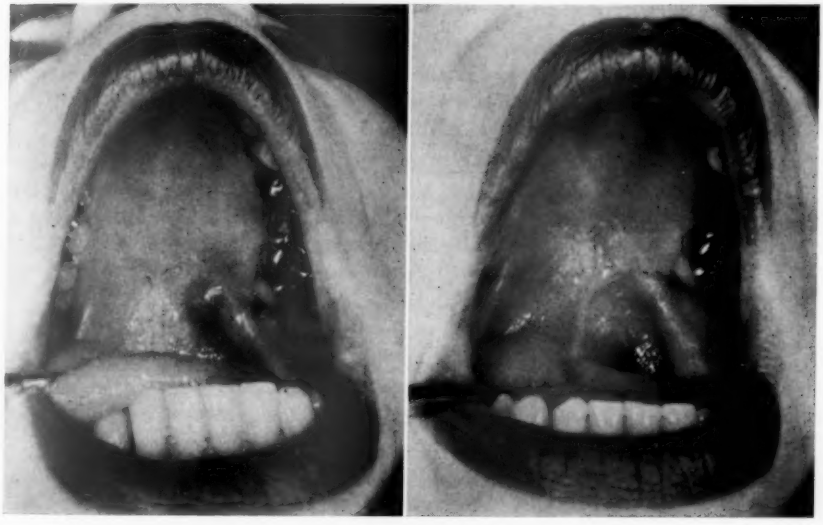
Case 4.—The case of a 10-year-old girl is interesting from another standpoint. This patient came under my observation on July 18, 1957, complaining of occasional pain. She stated: "About a month ago had a chill then got pain in the gum and swelling started inside."

Clinical examination revealed that the mandibular incisors were firm and the left incisor was discolored and open for drainage. The submaxillary and mental lymph nodes appeared normal to palpation.

With the history of trauma, the diagnosis of localized chronic osteomyelitis was easily reached after a study of the roentgenograms (Fig. 6). The patient responded readily to root canal therapy (Fig. 6), and after only seven months the periodontal lamella was mostly reformed.

The dentist had treated the case quite correctly. He reported the following findings of about two weeks previous: "Chief complaint was pain and swelling in the region of the mandibular incisors. Clinically, there was a boardlike swelling in the floor of the mouth, but no pointing. The pulp test revealed loss of vitality of the left central incisor. A blood count was ordered, which showed a slight increase in the eosinophil count." He was very much worried and suspected an eosinophilic granuloma or Hand-Schüller-Christian disease. The parents, informed of his suspicion, became quite alarmed and fearful that the child might have a serious illness. An increase in the peripheral esinophil count is not indicative of either of the conditions suspected by the dentists, and the undue alarm could have been avoided.

I wish to repeat that, clinically as well as radiographically, this was apparently a clear case of localized acute osteomyelitis. We all must be alert, of course, but there is no reason to look far and wide when a quite simple solution is at hand.



A. *B.*

Fig. 7.

CASE 5.—A 47-year-old woman was referred by her dentist on Jan. 27, 1958. She reported that at about the beginning of the month she had noticed a bump on the roof of her mouth. She thought it was irritation by something she had eaten and that it would disappear, since every now and then this had been the case. When she found that it was still there, she went to her dentist (a week before she was referred to my office) and he opened it. Fluid came out. The lesion turned black and was flat, but then it filled up again.

Clinical examination revealed a dark bluish mass, a little more than 1 cm. in diameter, raised about 2 mm. on the palate just at the posterior border of the hard palate and opposite

the last molar and slightly posterior to it. There was a suggestion of fluctuation. The mass was movable and was covered by normal mucous membrane (Fig. 7, *A*).

The dentist reported that the enlargement, when he saw it, was smaller than a dime (18 mm.) and the same color as the surrounding tissue. The aspirated fluid was straw colored and contained pus and blood.

At the time of my examination, blood and urine examinations were negative. Two days later the patient was operated on, under local anesthesia, in the office. With the radioknife, the tumor was circumscribed, except posteriorly, well within the normal tissues through the mucous and submucous layers and deep enough to reach below the mass. The mass was peeled out with the normal covering attached and intact. The posterior attachment was then severed with the radioknife drawn through normal tissue. Some dark blue venous-like blood (residue from the dentist's aspiration?) exuded during the operation. The tumor bed was cauterized and covered with sulfanilamide powder. The lips of the wound were approximated with five catgut sutures. Where this was not possible, Gelfoam was inserted. The closed wound was covered with sulfanilamide powder and with plain gauze which were to remain in position as long as possible. The specimen was sent to the laboratory of the New York Institute of Clinical Oral Pathology. Dr. Freund's diagnosis was as follows: "Muco-epidermoid tumor—well encapsulated—showing cellular activity." The patient was kept under observation until Feb. 4, 1958, at which time she had to leave the city. When she reported four weeks later, she had fully recovered. On April 1, 1958, when the patient was last seen the operative field looked quite satisfactory (Fig. 7, *B*).

Now let us study this case carefully. I am inclined to accept the patient's description of the lesion, except for the increase and decrease of the size before aspiration. However, the dentist's description of the aspirated fluid does not correspond with the histologic findings of a solid tumor.

Was it wise to aspirate at all? I do not think so. If it had been a mucous cyst (and of all the small tumors of the palate that I have seen, only one was a cyst), it would have had to be removed, for a cyst is not permanently cured by aspiration. What did the aspiration accomplish? Nothing but to obscure the diagnosis. It certainly looked like a hemangioma, a benign tumor. The mucoepidermoid tumor is on the borderline, and the safest treatment of a mass of this size is radical local removal without any previous interference of any kind. A characteristic finding of the usual type of tumor seen on the palate, namely, the mixed tumor of the salivary gland type,[1] is the suggestion of fluctuation to the palpating fingers, although such growths are solid tumors. Let me also repeat that the overlying soft tissue must never be dissected away and separated from the underlying tumor and utilized to close the wound, for in practically all cases this tumor invades the covering mucous and submucous layers. All these cases must remain under periodic observation. In fact, I tell all my patients, no matter what kind of operation they undergo, that they are never discharged and must communicate with me if something unusual occurs.

CASE 6.—A male patient in his seventy-sixth year was referred on July 11, 1956, for the care of exposed necrotic bone in the mandibular incisor region. He had undergone x-ray and radium treatment a few years previously for a squamous-cell carcinoma in the anterior region of the mandible. The oncologist's report follows:

> The patient had a perfectly characteristic squamous-cell epidermoid carcinoma on the anterior floor of the mouth extending over the alveolar border and between

two teeth that were in bad condition from infection, so that the growth actually extended on to the buccal side of the alveolar border. The laboratory report was that of a fully differentiated squamous-cell epidermoid carcinoma. We treated him by x-radiation beginning October 19 and carried through November 3, fourteen days in all of high-voltage x-radiation at 200 kv. and filtered by a number one thoraeus filter, which is the equivalent of 2 mm. of copper, approximately. Total dose over this fourteen day period was 2,100 r in air.

The next day, following completion of this radiation, radon seeds, eight in number, 1 mc.. each, and filtration 0.3 mm. of gold were implanted in and about the tumor-bearing area. The reaction was sharp and growth was controlled ultimately. Some of the low-grade osteomyelitis present in the first instance was undoubtedly aggravated by the radiation.

In consultation with the specialist, we agreed on conservative treatment of this diseased bone, removing only separated pieces of bone and permitting Nature to do most of the work. Roentgenograms taken at intervals showed the progress of separation (Fig. 8, July 11, 1956, and July 19, 1957). Only the important ones are shown here. However, extraoral and intraoral films were made a number of times in order that we might get a general view of the whole mouth to guide us in our attempt to put it into a healthy state while waiting for further development in the mandibular incisor and canine region.

The patient had complained of food getting in the "hole" (March 15, 1957). The fixed bridge had then been removed and a removable one constructed. The patient's dentist thought that the hole would fill in. We advised the patient to be sure to syringe the space after each meal to remove food debris and to prevent decomposition and the formation of foul odor. At this time the dentist wanted to close the opening over this necrosed bone with a soft tissue flap, but the patient took our advice (the specialist's and my own) when I explained the factors which speak against such a procedure.

A few months later hypergranulations formed mesial to the left canine. Being quite certain that these were not malignant I touched them with 8 per cent zinc chloride. A rhinologist happened to see the patient on July 18, 1957. He also examined the lesion and, believing that it was malignant, asked me to take a biopsy specimen. This I did after consultation with the specialist. All all the granulations were removed. They were examined by Dr. Freund, whose diagnosis read: "Inflamed granulation tissue and submucous hemorrhage. No evidence of malignancy found." We were all very much relieved.

The patient was seen frequently. The mouth was now in a fairly healthy state. Roentgenograms taken on Dec. 6, 1957 (Fig. 8), showed that we could attempt the removal of the sequestrum. On Dec. 9, 1957, two large sequestra were removed. They were later placed on an x-ray film, but no radiation effect was noticed on the developed film after a few weeks' exposure. The last intraoral films (Fig. 8, Dec. 18, 1957) revealed apparently healthy bone. This is further proved by the fact that from Jan. 29, 1958 to Feb. 24, 1958, when I last saw the patient, normal tissue could be seen covering the whole area. During this period two suspicious small areas—one on the labial aspect in the region of the lower left cuspid and another at the upper right central incisor—were removed for examination and found to be negative.

Such cases require much patience on the part of both the practitioner and the patient. When necrosed bone projects into the oral cavity because of recession of the surrounding soft tissue, the bone can be trimmed easily. It is difficult to understand how a dental practitioner can suggest covering necrosed bone with a soft tissue flap. Fortunately, this patient did not have much confidence in his dentist and was easily persuaded to not let him proceed.

Another important matter must be discussed, namely, biopsy. It happened that I was correct in considering the tissue to be nonmalignant. The

final diagnosis can be made only by microscopic examination, however, and I should have performed such an examination immediately. Here it must be repeated that small and readily removed masses are not to be biopsied but should be removed completely (excision biopsy).

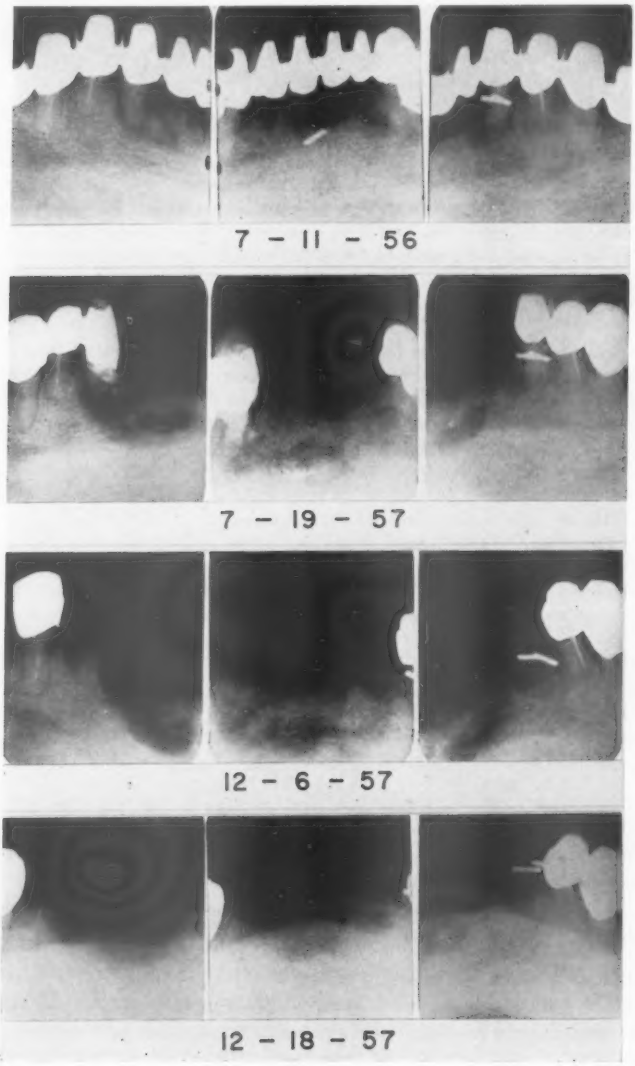


Fig. 8.

After the separated sequestrum has been removed, the exposed bone must not be curetted, since it is usually covered, at least in part, by soft tissue.

This is also seen in an ordinary osteomyelitis after the removal of a separated sequestrum.

A point pertaining to nomenclature comes to my mind now. Practitioners so often refer to a certain operation as "alveolectomy" as if it were possible to determine where the alveolus ends and where the adjoining bone of the mandible and the maxilla begins. Therefore, the term "alveolotomy," the cutting of alveolus, should be preferred. For the same reason, a sequestrum cannot be removed until it is separated from the healthy bone, since gross inspection cannot determine where the healthy bone begins.

One can only attempt to please everybody. Each of the cases reported carries one or more lessons. It has always been my experience that we become educated by our own mistakes—if we recognize them—and by the mistakes of others. We should be most grateful to each other, lenient in our criticism and understanding. A real teacher must know that nothing is gained by belittling a student. Kind advice and careful explanation are constructive.

I take this opportunity to discuss the matter of the oral surgeon versus the maxillofacial surgeon. An academic degree or degrees only connote fundamental training. I believe that the maxillofacial surgeon should be a graduate physician who has followed his training with internship and residency in surgery as well as with additional training in his special field. Malignant-tumor surgery should be practiced by the surgeon who is particularly equipped with knowledge of radiation therapy and all the other newer methods of handling such cases. If the maxillofacial surgeon is so trained, then malignant disease becomes part of his field. However, his domain does not include oral surgery cases involving extractions, impacted teeth, cysts, fractures, salivary calculi, etc. If the maxillofacial surgeons, the rhinologists, and the oral surgeons would stay within their respective fields, all the foolish resolutions that we read of lately would be unnecessary. One other thought: Why do some dentists who later receive a medical degree fail to include the D.D.S. among the other degrees on their stationery? Have they not acquired most of the knowledge of their specialty in the dental school? All this was an aside, but these problems are important.

What I still recommend and insist upon, however, is cooperation between general practitioners and specialists of both medicine and dentistry, for this cooperation benefits our patients.

REFERENCES

1. Blum, T.: Mixed Tumors of the Palate, Dental Cosmos 74: 943-953, 1932.
2. Blum, T.: Instructive Clinical Case Reports, Oral Surg., Oral Med. & Oral Path. 10: 1239-1253, 1957.

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THE TREATMENT OF ORAL HEMANGIOMAS

Report of Four Cases

Robert W. Christensen, D.D.S., Pasadena, Calif.

THE hemangioma is a tumor composed of blood vessels. It is formed from the endothelium of blood vessels and may take a capillary or cavernous form. It may be congenital, or it may form later in life. The hemangioma may gain considerable size and, when it does, may be very difficult to treat. Frequently a hemangioma will enlarge with age.

Hemangiomas may appear with some frequency in various regions of the oral cavity or face as well as in many other areas of the body. The hemangioma may be found arising in bone, but more frequently it arises in soft tissue areas and may then invade bone. It is most frequently found on the lip, tongue, and buccal mucosa, and it is found rarely on the palate.

Hemangiomas near the mucosal or epithelial surface are usually raised, lobulated, purplish-colored, compressible, and sometimes pulsating in character.

Usually the superficial tumors may be easily diagnosed by their general appearance and color. Also, by compressing the tumor between two fingers or against the underlying structures, we find that it loses its size but rapidly reshapes itself to its normal size. The hemangiomas in the deeper structures (muscles, glands, or bone) are much more difficult to diagnose, since discoloration may not be present and compression may not be feasible. Aspiration with a needle is a useful technique for diagnosing the more obscure hemangiomas.

Treatment of these vascular tumors may be by one or more methods, depending on the particular tumor's size, duration, location, and structural pattern and the age of the patient when the tumor first appeared. Treatment may consist of excision, irradiation, application of carbon dioxide snow, injection with a sclerosing solution, or a combination of these forms of treatment. I feel that surgical excision or injection of sclerosing solutions is to be preferred over irradiation in the oral region, especially in children. Possible radiation disturbances of the teeth and the bone-forming tissues should be considered seriously before irradiation therapy is decided upon as the treatment of choice. Certainly an attempt to control the growth or to decrease the size of these tumors should be made with the injection of a sclerosing solution, even if other types of therapy might need to be used later. Small, superficial, circumscribed lesions may be treated by excision.

Four cases of oral hemangioma will be presented. In one case (Case 1) the inadvertent injection of 0.5 c.c. of a radiopaque substance (Iodochloral) caused the hemangioma to become radiographically visible. The x-ray visibility of this tumor has increased as the tumor has regressed over the past twelve months due to the subsequent injection of a sclerosing solution. Although the injection of an oil-base radiopaque substance into a vein or artery is not an acceptable procedure for making these tumors visible, it nevertheless was useful in this case and, fortunately, was without sequelae. Two of the other three cases were treated by injection of a sclerosing solution, and one was treated by excision.

CASE REPORTS

CASE 1.—On March 3, 1958, J. R. H., a 6-year-old girl, was referred to my office for consultation regarding a large swelling of the right side of her chin and jaw which had been present one year.

Past History.—The patient gave the history of having consulted a physician a year before. He had observed the swelling as it enlarged and had attempted on two occasions to incise and drain it through an intraoral approach. Since bleeding ensued, he told the patient that this must be a "hematoma" due to some unknown earlier injury to the area.

After he had observed its steady growth pattern for a year, the physician decided that an exploratory operation via a submandibular incision was advisable to determine the true nature of the mass. At this time the patient's mother became concerned and visited another physician, who promptly referred the patient to the oral surgeon.

Examination.—The examination disclosed a well-nourished, pleasant, 6-year-old girl with a noticeable swelling of her right chin. The swelling measured approximately 5.0 cm. in a horizontal direction along the lateral aspect of the right anterior mandible. It measured 3.0 cm. vertically and seemed to bulge approximately 2.0 cm. laterally (Fig. 1). A very slight purplish discoloration was noted on the most pronounced lateral projection of the swelling (Fig. 2). To palpation, the mass had a firm, slightly fluctuant, grapelike texture; the mass was not attached to the skin surface and was slightly movable along its mandibular surface. The intraoral examination disclosed no pathology except a slight bulge and discoloration in the mucobuccal fold adjacent to the right deciduous cuspid and first molar. The mandibular central incisors were the only permanent teeth present. All the other deciduous teeth were present and in normal condition. There was no evidence of facial nerve disturbance or paresthesia of the mandibular or mental nerves of the right or left sides. To palpation the mass seemed to bulge just anterior to the mental foramen, then spread forward and inferiorly, and extend under the inferior border of the mandible. There was no appreciable compressibility of the tumor to digital pressure, but it could be moved slightly and seemed to be encapsulated. There was no pain to normal palpation. Pulsation was not perceptible to palpation or auscultation. Periapical and occlusal roentgenograms were taken of the mandible to rule out any bone or tooth pathology. These were negative. A tentative diagnosis of hemangioma was made, to be confirmed by an attempt to withdraw blood from the center of the mass by inserting a 20 gauge needle into it.

Treatment.—On March 3, 1958, the patient was given premedication of oral Seconal sodium, ¾ gr. and was allowed to lie down for forty-five minutes. She was placed on the operating table and draped and prepared in a routine fashion. A small amount of Xylocaine 2 per cent with 1:100,000 Adrenalin was injected for a right mandibular nerve block anesthesia. When the lip sensation had ceased, a 1⅝ inch, 20 gauge needle on a 2.0 c.c. syringe was used to enter the mass through the mucobuccal fold adjacent to the cuspid. At a depth of about 1.5 cm. the needle penetrated a large vessel, and with slight

retraction on the plunger the syringe was immediately filled with what appeared to be arterial blood. There was no noticeable spurting or pulsation of blood as it entered the syringe. At this point the nurse handed me another syringe filled, we thought, with 1.0 c.c. of sodium morrhuate. I removed the previous syringe containing blood from the needle, which was still in the vessel, and attached and injected 0.5 c.c. of the contents slowly into the vessel. At this moment I realized that although this solution looked like the amber-colored soapy solution of sodium morrhuate, it was really an oily solution instead. The nurse brought me the bottle and I then confirmed my belief that I had just injected the wrong solution—Iodochlorol. Fig. 1.

I quickly withdrew the needle and continued to keep finger pressure on the lower border of the tumor as it crossed beneath the mandible. I kept this pressure for fifteen minutes and observed the patient closely. There were no subjective or objective signs of untoward effects. I took two occlusal films of the mandible and referred the patient to a radiologist for films of the chest and mandible. The occlusal films taken at this time showed a roughly radiopaque mass in the shape of a mushroom, with its pedicle near the mandible and the curved top extending lateral to this (Fig. 9). The apex of the pedicle seemed to be about 1 cm. anterior to the mental foramen. The radiopaque mass seemed to have a smooth but convoluted external or lateral surface which extended approximately 2.0 cm. lateral to the mandible. The bulk of the tumor was approximately 5.0 cm. in anteroposterior direction extending from the second premolar to even with the central incisors. The mass was not homogeneously radiopaque but seemed to have strands of radiolucency running through the areas of radiopacity and giving it a cauliflower appearance. Fig. 3.

The posteroanterior mandibular view showed a well-demarcated, radiopaque mass lying at the lateral and inferior aspect of the right mandible just anterior to the visible mental foramen (Fig. 10). Its radiopaque areas seemed more dense than bone and were caused by the radiopaque substance. There was no visible extension of the contrast medium beyond the confines of the vascular tumor.

The lateral views of the mandible showed the contrast material filling the large vascular tumor whose bulk seemed to lie just anterior to the mental foramen and then swerve inferiorly and around the mandible in a posterior direction (Figs. 11 and 12). Fig. 5.

Roentgenographic Diagnosis.—Cavernous hemangioma, mental vessels filled with radiopaque contrast media. The chest film showed no presence of radiopaque contrast material in the chest or neck regions.

The patient was allowed to go home and was advised to rest. The next few days were uneventful. The patient's general condition was normal. On the fifth day following injection of the radiopaque contrast material, the patient was returned to the office for injection of the sclerosing solution. The patient was given premedication of Seconal sodium ¾ gr., and then a right mandibular nerve block injection was made in a routine fashion. A 22 gauge 1⅝ inch needle was inserted into the tumor mass from an intraoral approach until the needle was in the lumen of a blood vessel (Fig. 13). Sodium Morrhuate, 0.25 c.c., was injected slowly as strong finger pressure was exerted against the lowest border of the tumor to compress it against the inferior border of the mandible. The needle was now withdrawn from the lumen of the vessel and another 0.25 c.c. of the solution was injected into the stroma of the tumor. The needle was now withdrawn, and a small gauze sponge was held over the puncture wound for a few moments until bleeding had ceased. The patient felt no discomfort through this procedure. The patient was discharged to return one week later, at which time another occlusal roentgenogram showed that the tumor had decreased in size and that the contrast medium was now more dense (Fig. 14). Clinically, the tumor had decreased considerably. The tumor was now injected in a similar fashion with 0.5 c.c. sodium morrhuate. This time the needle did not puncture the vessel but was injected into the center of the mass. Fig. 7.

When the patient returned one week later, she and her mother were most relieved and thrilled to see the swelling on the chin so markedly reduced in size. It was now only

Fig. 1.

Fig. 2.

Fig. 3.

Fig. 4.

Fig. 5.

Fig. 6.

Fig. 7.

Fig. 8.

Fig. 1.—Case 1. Hemangioma causing swelling of right side of chin.
Fig. 2.—Case 1. Purplish discoloration of skin over tumor area is noted.
Fig. 3.—Case 2. Hemangioma of mucosa of cheek and lip.
Fig. 4.—Case 2. Disappearance of hemangioma following injection of sclerosing solution.
Fig. 5.—Case 3. Hemangioma of left mucobuccal fold area of oral cavity.
Fig. 6.—Case 3. Disappearance of hemangioma following injection of sclerosing solution.
Fig. 7.—Case 4. Small, pulsating hemangioma of lip.
Fig. 8.—Case 4. Disappearance of hemangioma of lip following total biopsy excision.

Fig. 9.—Case 1. Occlusal roentgenogram showing pedunculated mass filled with radiopaque material.

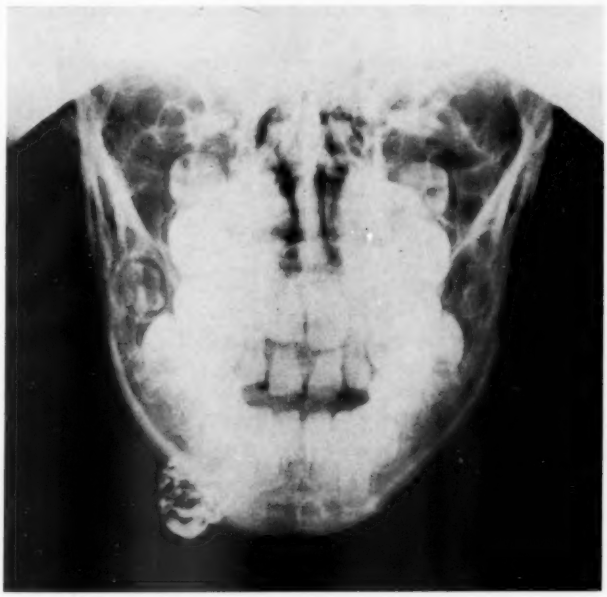

Fig. 10.—Case 1. Posteroanterior film of mandible showing position of tumor adjacent and inferior to right mental area of mandible.

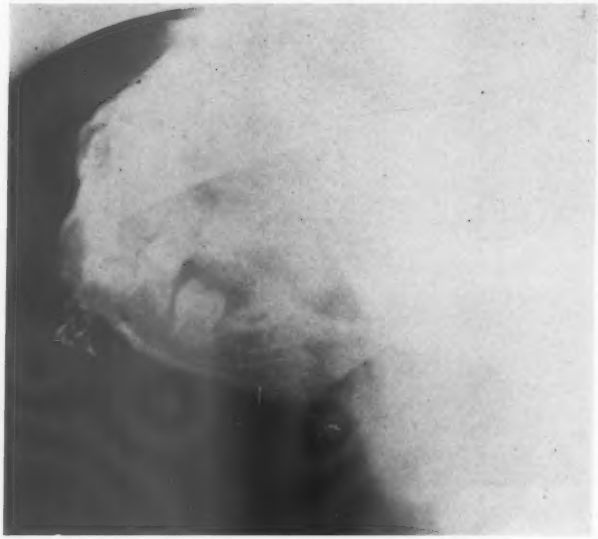

Fig. 11.—Case 1. Right lateral roentgenographic view of mandible showing position of tumor.

Fig. 12.—Case 1. Left lateral roentgenographic view of mandible showing how tumor extends off lateral aspect of right mandible.

one-third the size it had been at the time of our first examination. Occlusal films were again taken and showed the terrific reduction in the size of the tumor with a definite constricting of vascular spaces (Fig. 15). It was decided not to inject the tumor again, since it was now not noticeable, and to continue to observe it periodically.

Fig. 13.—Case 1. Needle is inserted into vessel.

Fig. 14.—Case 1. Occlusal film taken one week after first injection showing decrease in tumor size.

It has been observed and x-rayed periodically for one year, with complete disappearance of the mass to visualization and palpation (Figs. 16 and 17). There is no detectable presence of scar tissue in the area of previous tumor to palpation. Roentgenograms taken at

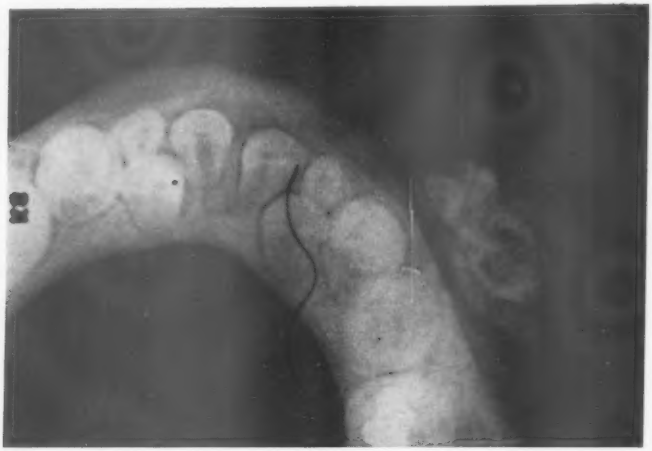

Fig. 15.—Case 1. Occlusal film taken one week after first injection showing massive reduction in tumor size.

Fig. 16.—Case 1. Occlusal film of tumor one year later. Tumor has nearly disappeared.

this time show the presence of a very small residual tumor mass still filled with radiopaque contrast material. Roentgenograms of the mandible and teeth show normal bone and tooth formation. This patient is entirely free of any presence of this tumor, and no further treatment is indicated or anticipated.

Fig. 17.—Case 1. Photographs of patient one year later with no visible tumor present.

CASE 2.—This patient was an 18-year-old private in the United States Marine Corps who was going through recruit training at the Marine base in San Diego. He was brought to the oral surgery clinic in May, 1951, with a hemangioma of the left inner commissure of the lip and adjacent buccal mucosa. This tumor was a raised, purplish, clustered mass which was soft and compressible (Fig. 3). It measured 2.5 by 2.0 cm. and had been present since the patient was 3 or 4 years old. It was raised approximately 8 mm. from the normal surface of the mucosa. On two occasions, one week apart, I injected the tumor mass with ⅜ c.c. of sodium morrhuate, and the tumor almost completely disappeared. The patient was observed for two months, and the postoperative photograph was taken (Fig. 4).

CASE 3.—The patient, a 32-year-old Negro woman, was referred by her general dentist on Jan. 25, 1957, because of a purplish tumor in the left lower mucobuccal fold adjacent to the lower first premolar. The tumor was a raised, purplish, soft, compressible, superficial mass lying in the mucobuccal fold (Fig. 5). It had been present as long as the patient could remember. It had enlarged in her youth but seemed to be static in growth since then. The patient had been warned against injuring the tissue because of the probability of uncontrollable hemorrhage, and she lived in fear of injuring it unknowingly. It took some persuasion to convince the patient that the tumor could be

made to disappear by injecting it. After she consented to the treatment, she was given two injections of 0.5 c.c. sodium morrhuate one week apart and the entire tumor seemed to disappear completely in one month. There was no palpable scar formation in the area of the previous tumor. She has been observed for the past two years without recurrence of the tumor (Fig. 6).

CASE 4.—The patient, a 53-year-old white man, sought professional advice regarding a "purplish bleb" on his lower lip. This tumor was a small, raised, circumscribed, pulsating blisterlike growth on the right lip at the mucocutaneous border (Fig. 7). It had been present since his youth and was a nuisance when the patient shaved. It was removed by total excision under local anesthesia, the attached vessels at its base being tied with one gut suture and the incision closed with 6-0 Dermalon. Healing was uneventful and without recurrence (Fig. 8).

DISCUSSION

The use of the sclerosing solutions to reduce the size of vascular tumors is a satisfactory form of treatment in many cases. It is not a particularly useful means of treating the lymphangiomas.[1] The lymphangioma is more susceptible and is better handled by surgical excision. It appears that the larger hemangiomas, once they are injected with a sclerosing solution, tend to continue their regression without many subsequent injections. It appears that as they tend to enlarge they can be made to regress, and once this regression begins it may go all the way. For this reason, I feel that the use of sodium morrhuate is very important in the management of this type of tumor. There does not appear to be any replacement of the original tumor area by cicatricial tissue. The various types of radiation therapy, I feel, should be used on widespread superficial tumors, or as a last resort, in order that there will be no injury to surrounding or adjacent tooth- and bone-forming tissues. Excision of smaller accessible hemangiomas is the treatment of choice.

SUMMARY

The types of treatment for hemangiomas occurring around or within the oral cavity are discussed. Excision of smaller, totally accessible vascular tumors is advised. The more obscure, larger, or deeper tumors may be better treated by sclerosing solution injections.

Four cases of hemangioma are presented. One case, because of the inadvertent injection of a radiopaque contrast medium into the afferent vessel of the tumor, was made radiographically visible. The effectiveness of injections of a sclerosing solution could now unmistakably be calculated and visualized. Two other cases of oral hemangioma were treated by injections of the sclerosing solution. All three patients were relieved of their tumors. One patient's hemangioma was treated by total excision. No recurrence was found in any of these cases. It is suggested that these two methods of treatment be given priority over radiation therapy in other cases of a similar nature.

REFERENCES

1. Christensen, Robert W.: Lymphangioma of the Tongue, ORAL SURG., ORAL MED. & ORAL PATH. 6: 593, 1953.
2. Thoma, Kurt H.: Oral Pathology, St. Louis, 1954, The C. V. Mosby Company.
3. Thoma, Kurt H.: Oral Surgery, St. Louis, 1958, The C. V. Mosby Company.

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PSYCHOLOGICAL REACTIONS TO ORAL CANCER

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ADVANCES in therapeutic techniques in the past few years have greatly improved the management of cancer patients, but at the same time they have altered the problems of clinical management. In surgical procedures, operative mortalities are no longer as great as they were in the past. Postoperative medical control has been improved to such a point that patients once considered inoperable are now suitable candidates for surgery.

A number of formal studies conducted by the Section of Research Psychiatry at Sloan-Kettering Institute and extensive clinical experience in the neuropsychiatric service of Memorial Hospital have led to the formulation of certain principles governing the behavior of patients with cancer. The cancer patient must be regarded as a person under a special and severe form of stress. The stress involved is usually multidimensional. Cancer is commonly perceived as an invariably fatal and loathsome disese having a cultural heritage of demonic proportions. For most people, it carries the threat of disability or death and, even after treatment, the omnipresent possibility of recurrence. In addition, there is usually the expectation of prolonged and intense pain. It is for these reasons that cancer constitutes an emotional stress of such enormity that it may threaten or disrupt important patterns of adaptation evolved by a person during the course of his development. A pattern of adaptation may be defined as a system of beliefs and behavior designed to bring the individual's physical and emotional needs into harmony with the demands of his environment. They include character defenses as well as the more positive striving for fulfillment of personal needs and are evolved early in the individual's life in response to environmental stimuli. Whenever a pattern of adaptation is threatened or disrupted, a considerable amount of anxiety is generated, for the individual may believe himself unable to meet environmental demands or to fulfill his own emotional needs.

Various body organs play significant roles in these basic adaptations. Early conflicts with parents may have centered around the use of an organ, or the organ could be secondarily involved in the solution of other conflicts. If cancer

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Supported in part by research grant No. M-1118, United States Public Health Service.

Address delivered before the Third Annual Cancer Seminar for Dentists, sponsored by the American Cancer Society, at the School of Dentistry, Fairleigh-Dickinson University, Teaneck, New Jersey, Jan. 12, 1958.

and its surgery threaten or remove the organ, it may disrupt an adaptive pattern. Such a disruption leaves the individual with a problem once again unresolved. It returns him to the setting in which the problem arose and in which the character defense or pattern of adaptation was first elaborated. If there is no disruption or if the individual can develop other compensatory patterns, then psychological difficulties are minimized. In fact, one can go so far as to say that neurotic or even frankly psychotic patterns of adaptation, if they are *not* disrupted by the disease or its treatment, actually may be assets in the restoration of the patient's emotional equilibrium.

The behavior of each patient should be considered as designed to prevent, avoid, minimize, or repair injury—not merely to a part of the body itself but also to the basic patterns and their inevitably wide social implications. The reactions to cancer and its therapy must be seen, therefore, as a sequence of related events which progress from the first time the individual notices something wrong with himself, through the climax of hospitalization and treatment, to convalescence and cure or to recurrence and death. The emotions and behavior are usually appropriate to the patient's view of what is happening to him and are designed to minimize or repair the damage inherent in those events. On the patient's first awareness of a body sign or symptom, a sequence of emotional reactions and related reality events begins to operate. The reality sequence can be characterized as consisting of four stages: the onset of symptoms, the diagnosis, the hospitalization, and the convalescence. Each phase of the sequence contributes to the patient's ability to integrate the total experience and, modified by his lifelong adaptations in living, sets the tone of ultimate posteancer functioning.

For this audience I shall devote the major portion of my remarks to the preoperative or anticipatory phase of the experience. Oral cancer is a problem of increasing significance to the dentist; it accounts for 70 per cent of the cancers of the upper alimentary and respiratory tract. Of all human cancers, 4 per cent occur in the mouth. Since mouth lesions are often unsuspected by the patient, the burden of their detection and the necessity for communication of this fact to the patient frequently fall upon the shoulders of the dentist, although some patients may become aware of the symptom themselves and come to the dentist for help. In either event, the patient's first awareness of oral disease initiates a chain of interrelated psychological reactions. These reactions are modified by experiences during the course of diagnosis and treatment. There is no single and unchanging reaction based upon a "character type" or any other nosological entity. The events and experiences in therapy are sequential, and the responses to the phases of treatment also form a sequence. The responses of patients to each phase are shaped by the nature of the immediate events as well as by previous life experiences.

The most prominent psychological reaction aroused by the awareness of "something wrong" is anxiety. Immediate anxiety is extremely painful, and some course of action is necessary to diminish its intensity. The course of action pursued by each patient is determined by his perception of the magnitude of

the threat and by his inventory of resources, both real and subjective, for mastering the threat effectively. The course of action undertaken by each patient, therefore, must be entirely individual.

The patient often has a fund of knowledge concerning signs, symptoms, and treatment of cancer. This factor often influences his reactions to the symptoms. When a member of the patient's family has had oral cancer, with a difficult postoperative course or an ultimately fatal outcome, the patient is likely to assume that such is the unavoidable course of the disease. This biased knowledge increases fear and disrupts the patient's early efforts to integrate the threat and to institute effective action.

If the symptom does not arouse disorganizing fear, consultation will be sought immediately in a realistic effort to meet the threat. On the other hand, if excessive fear is aroused, the patient may deny the existence of the symptom or avoid seeking medical care when he does recognize its implications. Both denial and avoidance serve to delay early care, a factor so vitally important in cancer therapy. Avoidance and denial are psychological mechanisms which function to reduce anxiety in a situation of threat. Avoidance is an inhibition of action in the face of threatening knowledge, whereas denial is an inhibition of knowing to prevent emotional disorganization. Therefore, delay in seeking medical care can be regarded as the first indication of efforts to forestall what the patient anticipates as certain disaster. In a sense, the fear aroused by the symptom may be so intense that the patient is virtually immobilized. As an illustration of the function of such a mechanism, I should like to quote a statement by a radical-mastectomy patient who delayed six months before she could seek medical care:

> In the summer I felt an annoying feeling but no pain. In September I noticed that my nipple was a little funny. I showed it to my husband and went to a doctor this month (February). Maybe if I had gone in the summer it would be over with by now. I didn't think it was anything at all. I generally don't examine my breasts. I don't go around pushing and feeling. Not like some people who are always looking for something wrong. But I always had a fear of cancer. It has always been a great fear with me. Just like I fear being caught in a fire. Those have always been my two great fears, cancer and being trapped in a fire.

In describing her behavior and feelings in relation to her symptom, the patient revealed the essential factors in her delay. Awareness of a symptom materialized a lifelong symbolic fear, thus placing her in an intolerable position similar to being "trapped in a fire."

It should not be assumed, however, that patients who take action immediately on becoming aware of the symptom may not have a potential of avoidance or denial. Casual observation of patients who seek care immediately often will not reveal that they have taken action only because of some environmental circumstance, such as pressure or insistence of a family member. Furthermore, there are many patients who apparently seek care early and yet may still be terrified, even if they have not communicated their fear directly or exhibited disruptive behavior. It is extremely important to determine the patient's

earliest feelings with regard to the symptoms if we are to understand subsequent emotional requirements. Such understanding is vital in the successful management of a patient with oral cancer.

For the dentist, informing the patient of the necessity for a biopsy is the most common and difficult problem. With all its implications, this information is never easily conveyed or calmly received. Patients may report being "shocked," "terrified," "numb," "panicky," or "stunned." Nevertheless, the impact can be lessened when the relationship between the dentist and his patient is such that the dentist is seen as a warm, supportive figure rather than as one who is threatening and hostile. In fact, the manner in which information is given is just as important as the specific content. More succinctly put, the "how" of telling is as important as "what" is told.

The nature of the information given to the patient usually depends on the interaction between the dentist's convictions about cancer and imparting information to the cancer patient and the patient's insistence on being told details. It is here that the dentist-patient relationship reaches its crucial test. If this is handled poorly, the patient will experience an increase in anxiety and in some instances will develop serious mistrust of the dentist and of all medical authorities who follow him. Either of these feelings will have a profound influence on the patient's entire pre- and postoperative course. The dentist should be prepared to spend considerable time with such a patient, interpreting the need for biopsy and encouraging the patient to express feeling and fears freely so that distortions and misconceptions may be identified. In addition, he will find that the patient's specific psychological difficulties will become quite evident. As a result, the dentist-patient relationship is decidedly strengthened and affords a basis for helping the patient later when the dentist communicates his knowledge to the specialists with whom the patient will have future contacts. It cannot be emphasized too strongly that an hour of permissive discussion when the need for biopsy is interpreted or when the diagnosis is established can be more advantageous to the patient than months of psychotherapy during and after convalescence.

The patient's response should be, at all times, the ultimate determinant of what information should be given. The patient usually indicates how much knowledge he wants or can tolerate by what he says and by the questions he asks. There is one common pitfall to be avoided. Although the patient may state that he wants the whole truth, the request only too frequently masks a terrified demand that he be told that there is nothing seriously wrong with him. A course must always be steered between terrifying obscurantism and equally terrifying and unabsorbable information. Forcing the patient to accept more information than he can tolerate frightens him to the point of serious disorganization.

Let us consider for a moment the enormous psychological significance of the oral cavity. In early infancy the oral zone is of great importance, since the child receives nutritive gratification through this medium and experiences the mouth as a source of sensory pleasure, as in sucking, and exploration. In early life the infant also influences the world around him by using his mouth for

crying, refusing to eat, or biting. As he gets older, the child continues to refine the uses of his mouth in the techniques of living. He may use it as a weapon of defense, as in arguing or attacking with words. As he continues to develop, the mouth takes on other meanings and is used to express tender emotions and sexual feelings as well as rage and determination. In all persons, residua of early oral behavior persist into adulthood in a modified, socially acceptable form.

Any or all of these factors may play a role in the psychological world of a given patient with symptoms of oral cancer. I can say without reservation, however, that the possible loss of the ability to communicate with others is the outstanding focus of anxiety. For most, language and speech are the primary avenues for human relatedness. Any experience which threatens to compromise this function cannot be borne lightly. A threat to this particular function often raises the specter of social isolation and separateness from other human beings. I am certain that all of you have seen the profound upsurge of fear and anxiety in patients when multiple extractions are deemed necessary. Detection and biopsy of mouth lesions is perhaps a situation of even greater anticipatory terror. As a further complicating factor, the fears may be conditioned by early experiences with dentists and cause a reactivation of early traumatic events that occurred at a time when as a child the patient was realistically helpless and may have projected to his dentist the image of his father in whatever way happened to fit his own psychological climate.

Paradoxical though it may seem, a supportive dentist may find the patient ventilating hostility and resentment toward him. Usually this means that the patient feels secure enough in the relationship to release the suppressed feeling. The dentist should meet this test of trust with acceptance and understanding. When the medical authority becomes impatient and angry, the patient's anxiety increases, and fantasies of retaliation at the hands of the more powerful authority result. It is doubtful that it will ever be possible to develop an absolute and infallible plan to apply uniformly in the relationship with any cancer patient. The most fruitful approach is for the dentist to focus entirely upon the patient's feelings and attitude and thus establish a significant relationship. Acute anxiety, to which a distant or hostile person invariably contributes, rather regularly results in gross distortions of fact. The only useful guide to the patient's ability to handle anxiety is determination of the meaning of the experience to him. The rather moralistic fashion of dividing personalities into the mature and the immature, the normal and the neurotic seems to have less and less meaning as our understanding of the dynamics of adaptation deepens. More and more, these appear to be abstract entities better designed to fit into theories than to describe real persons. They add nothing to our understanding of dynamic processes. The emphasis should be placed on understanding the meaning of the specific experience to the individual patient in his total life adaptation rather than to an abstract personality type that can withstand any experience abstractly regarded as stressful.

One word about planning for the use of a prosthesis as an integral part of management of the cancer patient: The dentist should have all current information available regarding the most recent prosthetic advances, and he should counsel his patients about them. Many patients have gross misconceptions about prostheses, and it is incumbent upon the dentist to search out those distortions, to correct them, and to interpret prostheses in a reassuring but realistic manner.

I have elaborated in some detail at least a part of the total experience of the cancer patient, with particular emphasis on the preoperative or anticipatory phase. The sequence of events and the related emotional changes attest to the difficulty of speaking of a generalized and abstract concept of cancer. Of necessity, we must consider each patient as an individual with a particular type of cancer, who has undergone or is undergoing a particular form of surgery or other therapy. There is no special psychology of patients in whom cancer develops. Cancer happens to all types of people and does not, as far as we know, select individuals with particular kinds of emotional problems. Moreover, cancer itself is not a uniform disease. It can vary from a basal-cell carcinoma with almost no possibility of mortality to a highly malignant, rapidly growing tumor which defies all methods of control. Cancer can necessitate the removal of almost any organ of the body, organs which play varying roles in the total life adaptation of the patient even before the onset of the illness. One cannot, therefore, easily separate adaptation to cancer from adaptation to measures needed for its cure. As we have seen, the adaptations which occur are by no means static. Actually, the adaptations begin with the patient's discovery that something is wrong with him, they progress for better or worse in the preoperative course to the culmination and crisis of surgery, and then they evolve during postoperative convalescence toward a long-range, more or less final resolution. In addition, they are not at any time independent of concurrent life situations; on the contrary, those concurrent life situations and the patterns of adaptations achieved during the illness fundamentally influence each other.

There appears to be an assumption currently held that the only real problem is the patient's belief that he has problems. This assumption results in an attempt to dissuade the patient that he has a problem or at least to minimize the problem. Even when one is fortified with all the usual clichés, this approach is rarely effective because it is totally unrealistic. The patient has very real and very immediate problems to solve which must be solved by him or with the help of others, but if the patient is to return to his previous level of functioning and emotional peace, his problems must be solved.

Unfortunately, we do not now have the means to predict who will do well psychologically and who will not do well. We cannot assume that a prediction can be based on the patient's position on some psychiatric diagnostic scale. We cannot even make a prediction of the ultimate adaptation of a patient on the basis of his grosser adaptation, that is, whether or not the patient seems to be a "well-balanced individual." We have to know exactly

how this experience integrates with or disrupts his major patterns of adaptation. I believe that this is usually far too subtle to be determined with any degree of accuracy before the actual event occurs.

In conclusion, it is my opinion that we must be entirely realistic and appreciate the emotionally disruptive nature of cancer detection and therapy, particularly when an organ of great psychological significance is involved. Patients with cancer need understanding support during every step of their experience with the illness if they are to meet the threat of the situation with adaptability. If this support can be routinely forthcoming to all patients, then they may be spared intense emotional reactions and psychologically determined limitations in living after they are cured. The cured cancer patient can live an effective life, but only if we accept our obligation to aid in the process of reducing trauma and restoring function.

REFERENCES

1. Bard, M., and Sutherland, A. M.: Psychological Impact of Cancer and Its Treatment. IV. Adaptation to Radical Mastectomy, Cancer **8**: 656-672, 1955.
2. Bard, M., and Dyk, R. B.: The Psychodynamic Significance of Beliefs Regarding the Cause of Serious Illness, Psychoanalyt. Rev. **43**: 146-162, 1956.
3. Bogdonoff, M. D.: The Effect of the Physician's "Psyche" Upon the Patient's "Soma," Ann. Int. Med. **46**: 886-892, 1957.
4. Finesinger, J. E., Shands, H. C., and Abrams, R. D.: Managing the Emotional Problems of the Cancer Patient, CA—Bull. Cancer Progr. **3**: 19-21, 24-31, 1953.
5. Sutherland, A. M.: Psychological Barriers to Rehabilitation of Cancer Patients, Postgrad. Med. **17**: 523-526, 1955.
6. Sutherland, A. M.: Psychological Impact of Cancer and Its Therapy, M. Clin. North America **40**: 705-720, 1956.
7. Sutherland, A. M.: Psychological Factors in Surgical Convalescence, Ann. New York Acad. Sc. **73**: 491-499, 1958.
8. Sutherland, A. M., and Orbach, C. E.: Psychological Impact of Cancer and Cancer Surgery. II. Depressive Reactions Associated With Surgery for Cancer, Cancer **6**: 958-962, 1953.

EXODONTIA

FLUID BALANCE AFTER MULTIPLE DENTAL EXTRACTIONS AND ALVEOLOPLASTY

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WHILE it is generally accepted that disturbances in fluid balance play an important role in surgical shock, postoperative morbidity, and the healing of wounds, no reference to the study of fluid balance can be found in the dental literature. Recently, impetus has arisen with regard to surgical blood loss. The present preliminary study was instigated to assess the status of fluid balance associated with oral operative procedures for multiple dental extractions and alveoloplasty.

In reviewing the literature, it becomes apparent that maintenance of the internal environment depends on a complex physiochemical equilibrium. Baird and Stembridge[1] stated that dehydration is not a single entity but, rather, a finding common to two syndromes—depletion of water and depletion of electrolytes—which are dissimilar in all major characteristics. The present study was approached strictly from the standpoint of water, or fluid, balance, with no attempt at evaluation of electrolytes.

Most patients recovering from the trauma of oral operations are able to consume fluids; therefore, one of the prime concerns was to determine as accurately as possible the daily state of hydration of these patients when they were allowed to partake freely of liquid nourishment according to their desires. Another objective was to obtain some estimate of the obligatory water loss and daily water requirement.

Daily water metabolism was divided into four components[2]: water intake, metabolic water,* urinary output, and insensible water loss. "Absolute losses," such as vomitus, sputum, blood, and other abnormal losses, have no physiologic

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Abridgment of thesis submitted by Dr. Bergan to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Dentistry.

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*The term "metabolic water"[3] includes the water of oxidation and the preformed water of catabolized protein, fat, and carbohydrate.

function and must be recorded for inclusion in calculation of water requirements as a fifth component.[4] The daily fluid balances in our study were calculated from these data.

The ratio of water to solute in blood serum, or the "serum water concentration," has been investigated recently.[5-8] Its value as an indication of the status of the body water was scrutinized by Sturtz.[9] A collateral aim in this study was to evaluate the merit of determining the serum water concentration in patients after oral operations.

CLINICAL MATERIAL AND METHODS

The fluid balance was analyzed in fourteen adult patients after multiple odontectomy with alveoloplasty. Complete mandibular and maxillary odontectomy was performed on every patient except one, in whom the mandibular incisors were retained. The number of teeth extracted varied from twenty to thirty-one per person, and the extent of the alveoloplasty ranged from grades 1 to 4.[10] Every patient had diverse degrees of periodontal and periapical infection. The group included seven men and seven women, ranging in age from 39 to 73 years; the majority were in the fifth and sixth decades of life.

All patients had a thorough physical examination, with special emphasis on their status as good anesthetic risks and on the absence of any systemic afflictions that might interfere with the normal physiologic function of body fluids and the balance mechanism. The patients were studied under isolated and close observation. Clothing consisted of cotton sheets and one medium-weight wool blanket, and the room temperature ranged from 72 to 76° F.

Solids were not ingested after 9 o'clock on the evening before the operation; to minimize any anesthetic complications and postoperative nausea or vomiting, liquids were not allowed for at least five hours before operation. Each patient was weighed nude on the morning of operation and again at two consecutive twenty-four hour intervals. Body weight was measured on a kilogram platform scale that had been calibrated to within ± 10 grams with known weights.

Premedication was kept constant and consisted of the intramuscular injection of ⅙ gr. (10 mg.) of morphine sulfate and $\frac{1}{150}$ gr. (0.4 mg.) of atropine sulfate thirty minutes prior to operation. Anesthesia was induced by the intravenous injection of a 2.5 per cent solution of thiopental (Pentothal) sodium and maintained by combining the intravenous injection of Pentothal and the inhalation of a mixture containing 70 per cent nitrous oxide and 30 per cent oxygen after nasal endotracheal intubation under the effect of succinylcholine chloride. The quantities of Pentothal used ranged from 20 to 40 ml. (500 to 1,000 mg.), and the average length of each operation was approximately one hour and twenty minutes.

A total of 4 ml. of a 2 per cent solution of lidocaine hydrochloride with 1:100,000 epinephrine was infiltrated into the labiobuccal vestibule of each dental arch in an attempt to produce some hemostasis. Every surgical procedure was standardized to make all operations as nearly identical as possible. The mucoperiosteal flap-forceps technique, followed by rongeur-file alveoloplasty,

débridement, and closure with continuous silk sutures, was uniformly employed. All intake and output during operation, including that represented by abnormal losses, such as saliva, aspirated blood, blood-saturated sponges, teeth, and débridement, were accurately weighed, saved for later calculation, or both.

Specimens of blood and urine were obtained preoperatively and at successive intervals of seven, fourteen, twenty-four, thirty-one, thirty-eight, and forty-eight hours. The urinary output and all fluid intake were double-checked for weight; in some instances, the daily excretion of nitrogen was determined. Only three stools were passed in the twenty-eight patient-days of the study; these were weighed directly. All abnormal postoperative losses were weighed or calculated and recorded. The scale used to weigh all intake and output was calibrated to within ± 0.1 gram, and all data were charted as to type, weight, and respective time.

The diet was made as liquid as possible and of such composition that it was somewhere between the usual mixed diet and a high-carbohydrate supermaintenance diet.[3] This allowed an approximation of the percentage of insensible loss of weight due to insensible loss of water.

All evidences of perspiration, apprehension, anxiety, hyperactivity, nausea, vomiting, and other factors that might influence insensible water loss were noted in each patient.

All data were expressed in terms of 1 square meter of body surface per twenty-four hours. As suggested by Talbot and associates,[6] this gives uniformity and makes the data applicable to patients of all sizes and ages. Nomograms constructed from the equation of Du Bois and Du Bois[11] were used to calculate the surface area from the patient's weight and height. In this study, everything possible was weighed on the gram basis, and all fluids were assumed to weigh 1 gram per milliliter.

The amount of blood lost during operation was calculated by determining the hemoglobin content of the collected materials colorimetrically with the Sheard-Sanford photelometer,[12, 13] employing the modified technique of Gores.[10]

The osmolarity* of all samples of serum and urine was obtained by the freezing-point depression, using a Fiske osmometer[14, 15] and according to the method of Crawford and Nicosia.[16] The serum and urinary water concentrations then were calculated by dividing 1,000 ml. by the number of milliosmols in the tested sample; the units obtained were milliliters of water per milliosmol of solute.[9]

The total urinary excretion of solutes was calculated by multiplying the urinary volume (milliliters) by the urinary osmolarity (milliosmols per 1,000 ml.). The urinary volume, or weight, and urinary water were assumed to be identical, and no correction was made for urinary solids. This introduced a small systematic error that was constant throughout.[9]

Obligatory urinary water was calculated on the assumption that the average minimal urinary water concentration in a postoperative patient who does not

*"Osmolarity," the term in common usage, has been employed in this paper in preference to the more accurate term "osmolality."[9]

have renal or endocrinologic disease is 1 ml. per milliosmol.[9] Then, by multiplying the total urinary excretion of solutes (milliosmols) by 1 ml. per milliosmol, the volume of obligatory urinary water was obtained in milliliters. The difference between the total urinary volume and the obligatory urinary volume equaled the free urinary water.

The following equation

beginning weight – (end weight – ingesta + excreta[17])

was used to determine weight loss, and the insensible water loss was taken as 90 per cent of the insensible weight loss.[18]

The figure of 270 ml. per square meter of body surface per day has been advocated by several authors[2, 3, 19] as the daily metabolic water rate. This was substantiated by Sturtz,[9] who obtained a metabolic rate of 276 ml. per square meter per day. All these metabolic water rates were determined on patients being nourished solely by infusions of dextrose. The patients in our present study, however, were maintained on protein, fat, and carbohydrate given orally. The metabolic water was calculated daily on twelve of the twenty-eight patient-days in our study according to the method of Wiley and Newburgh.[20]

RESULTS

Daily Body Weight (Table I).—The variation in body weight was from –1.175 to +0.561 kg. per square meter per day, with mean values of –0.599 on the first day, –0.294 on the second day, and –0.469 for both days. Every patient lost weight, except for the patient in Case 3 in whom a slight gain in weight occurred on the second day.

TABLE I. CHANGES* IN BODY WEIGHT AND URINARY EXCRETION OF SOLUTES AFTER ORAL OPERATIONS

CASE	CHANGE IN BODY WEIGHT				TOTAL EXCRETION OF SOLUTES (MILLIOSMOLS/SQ.M./DAY)	
	KG.		KG./SQ.M./DAY			
	FIRST DAY	SECOND DAY	FIRST DAY	SECOND DAY	FIRST DAY	SECOND DAY
1	-1.665	-0.805	-0.757	-0.336	446	240
2	-1.160	-0.500	-0.682	-0.294	363	304
3	-1.740 (H)	+0.970 (L)	-1.006	+0.561 (L)	478	558
4	-0.720	-0.270	-0.490	-0.184	297	327
5	-1.680	-0.610	-1.175 (H)	-0.427	609 (H)	451
6	-1.440	-0.410	-0.857	-0.244	527	363
7	-0.150	-0.350	-0.081	-0.190	494	520
8	-1.562	-1.038	-0.746	-0.676	368	430
9	-0.500	-1.120	-0.244	-0.546	339	391
10	-0.730	-0.370	-0.514	-0.261	304	594
11	-0.340	-0.710	-0.200	-0.418	316	479
12	-1.300	-0.840	-0.756	-0.488	374	471
13	-0.810	-1.210	-0.405	-0.605	254	266
14	-1.020	-1.240	-0.486	-0.590	209 (L)	426
Mean	-1.058	-0.575	-0.599	-0.294	384	416
Mean of 2 days	-0.817		-0.469		400	

*H = highest; L = lowest.

Insensible Water Loss (Table II).—The mean insensible water loss was 609, 688, and 642 ml. per square meter per day for the first day, the second day,

and both days, respectively. The range was from 384 to 1,107 ml. per square meter per day. Seven patients showed a greater insensible water loss on the first day than on the second day; this difference was slight in all but the patient in Case 10, in whom the loss on the first day was considerably greater. The remaining seven patients had greater losses on the second day; in Cases 5 and 7, the loss on the second day was at least twice that on the first day.

TABLE II. DATA* ON WATER BALANCE (ML./SQ.M./DAY) AFTER ORAL OPERATIONS

CASE	DAY	INSENSIBLE WATER LOSS	TOTAL URINARY VOLUME	ABNORMAL LOSSES	TOTAL LOSSES	WATER INTAKE	METABOLIC WATER	TOTAL GAIN	WATER BALANCE
1	1	812	695	320	1827	1204	160	1364	-463
	2	1107 (H)	580	32	1719	1477	160	1637	- 82
2	1	518	775	1037 (H)	2327	1754	160	1914	-413
	2	567	1397	18	1982	2015	160	2175	+193
3	1	555	542	250	1347	438 (L)	160	608 (L)	-745
	2	454	830	19	1303	1913	160	2073	+770 (H)
4	1	727	323 (L)	282	1332	959	160	1119	-213
	2	765	515	43	1323	1223	160	1383	+ 60
5	1	406	622	673	1701	609	160	768	-932 (L)
	2	812	555	22	1389	1053	160	1213	-176
6	1	805	485	697	1977	1254	244† (H)	1280	-563
	2	744	613	20	1377	1217	144†	1343	0
7	1	384 (L)	905	93	1382	1369	128†	1511	+147
	2	896	1439 (H)	17	2352 (H)	2262 (H)	213†	2319 (H)	+ 70
8	1	555	432	679	1666	1005	151†	1124	-501
	2	593	946	21	1560	1116	144†	1242	-284
9	1	734	517	307	1558	1427	176†	1521	+ 29
	2	677	757	16	1450	978	115† (L)	1133	-312
10	1	757	342	1008	2107	1699	157†	1818	-248
	2	427	1010	21	1458	1318	156†	1432	+ 20
11	1	547	519	245	1311	1200	128†	1342	+ 49
	2	650	1302	19	1971	1626	160	1786	-204
12	1	692	1096	220	2008	1364	160†	1524	-484
	2	572	1007	19	1598	1173	160	1333	-265
13	1	460	691	201	1352	1029	160	1189	-163
	2	410	1015	15	1440	945	160	1105	-335
14	1	574	420	93	1087 (L)	686	160	846	-241
	2	570	768	13 (L)	1351	1021	160	1181	-170
Mean 1st day		609	597	436	1642	1143	163†	1281	-339
Mean 2nd day		688	910	21	1591	1381	155†	1525	- 51
Mean of 2 days		642	754	229	1616	1262	160†	1403	-195

*H = highest; L = lowest.
†Individually calculated metabolic water.

Total Urinary Volume (Table II).—The daily output of urine was about 50 per cent greater on the second day than on the first day, with mean values of 910 and 597 ml. per square meter per day, respectively. The over-all average for the study was 754 ml. per square meter per day, and the extremes were from 323 to 1,439. The urinary excretion of solutes is important, since it is

the prime factor in determining the daily obligatory urinary volume. The patients in this study were under some stress, so Sturtz's[9] value of 1 ml. per milliosmol was employed as the minimal urinary water concentration rather than the lower value of 0.7 ml. per milliosmol set up by Gamble and other investigators.[21, 22] Thus, the figures for total excretion of solutes (milliosmols per square meter per day) in Table I could be considered as the obligatory urinary volume (milliliters per square meter per day). The mean values of both of these items were 384 on the first day and 416 on the second. The average for the twenty-eight patient-days was 400, with the highest value being 609 and the lowest being 209. Comparison of the daily values of the obligatory urinary volume with those of the total urinary volume (Table II) revealed that only one patient (Case 6, during the first day) was concentrating urine consistently to less than 1 ml. of water per milliosmol per day.

Abnormal Losses (Table II).—Surgical blood loss and emesis comprised the bulk of the abnormal losses, with blood loss predominating. The mean values were 436 ml. per square meter for the first day, 21 ml. per square meter for the second day, and 229 ml. per square meter per day for both days. The range for the first day was from 93 to 1,037 ml. per square meter, but for the second day it was only from 13 to 43. Thus, abnormal losses represented an important component in the determination of the fluid balance in this particular study.

Water Intake (Table II).—The mean values for the intake of water (milliliters per square meter per day) were 1,262 for the twenty-eight patient-days, 1,143 for the first day, and 1,381 for the second day. Five of the first-day averages were greater than the respective second-day averages. The range was from 438 to 2,262, with the majority of values being between 1,000 and 1,500.

Metabolic Water (Table II).—The mean metabolic water determined from twelve daily calculations was approximately 160 ml. per square meter per day. The lowest value was 115, and the highest was 244. The average for both days (160 ml. per square meter per day) was utilized as the daily value for metabolic water in all cases in which metabolic water was not calculated directly. This metabolic water included the water of oxidation of the ingested carbohydrate, protein, and fat and any catabolized fat or protein, plus the preformed water associated with the last two. Since it was impossible with this calculation to know how much tissue carbohydrate was catabolized, this amount was assumed to be nil and was not included in the final calculations. It also was assumed that the kidneys adequately cleared all the nitrogen presented to them and that any nitrogen excreted in the feces was negligible.[23]

Water Balance (Table II).—Comparison of the total daily gains and losses of water gave the water balance. Eleven patients had negative water balances on the first day, and eight had negative balances on the second day; thus, nineteen of the twenty-eight daily balances were negative. One daily balance was zero. Mean values of –339, –51, and –195 ml. per square meter per day were found for the first day, second day, and both days, respectively. The greatest negative water balance was –932 ml. per square meter per day, and the largest positive water balance was 770.

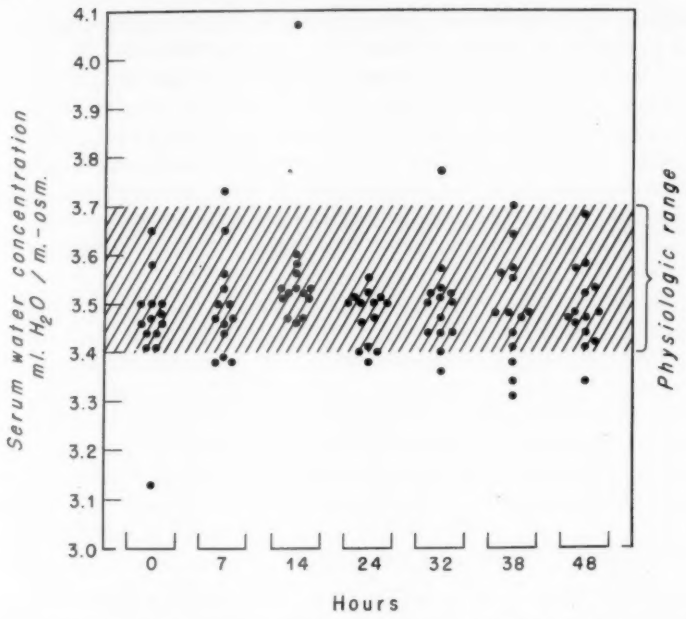

Fig. 1.—Values for serum water concentrations measured during ninety-eight observations in fourteen patients after oral operations.

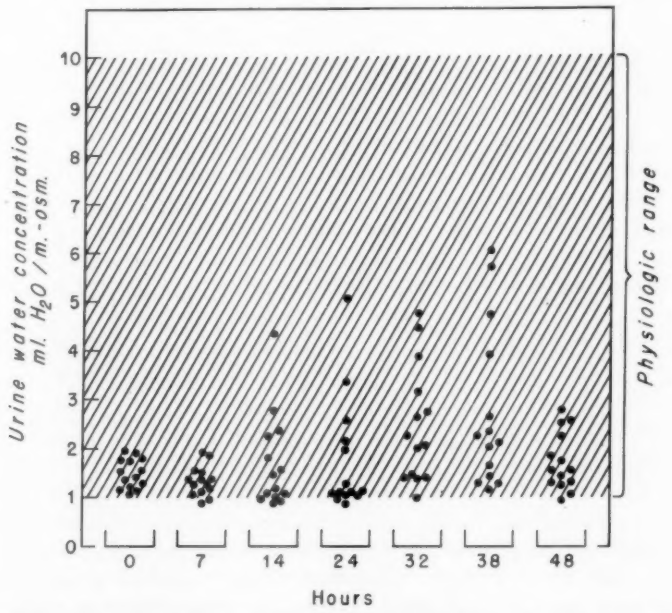

Fig. 2.—Values for urinary water concentrations measured during ninety-eight observations in fourteen patients after oral operations.

Serum and Urinary Water Concentration.—Talbot and associates[5-8] established the physiologic limits of serum water concentration as 3.5 to 3.7 ml. of water per milliosmol of solute. Sturtz[9] lowered the minimum to 3.4. In this study, the serum water concentration in sixty of eighty-four periods of approximately eight hours each was the same as or less than Talbot's physiologic minimum, while only twelve periods showed a serum water concentration that was the same as or less than the physiologic minimum set by Sturtz (Fig. 1). Four periods showed concentrations at or above the physiologic maximum. The lowest serum water concentration was 3.13 ml. of water per milliosmol, and the highest was 4.07.

The urinary water concentration for a like number of periods ranged from 0.87 to 6.06 ml. of water per milliosmol (Fig. 2). None of these results were outside the physiologic limits of 0.7 to 10 ml. of water per milliosmol set by Gamble and Butler,[21] but there were ten periods during which the urinary water concentration was less than 1 ml. of water per milliosmol, the physiologic minimum advocated by Sturtz.[9] Thirty of the periods showed values greater than 2 ml. of water per milliosmol; thus, the majority of the urinary water concentrations were between 1 and 2 ml. of water per milliosmol.

COMMENT

Daily Body Weight.—The consistent loss of weight in twenty-seven of the twenty-eight daily determinations suggested that patients recovering from this operation were in a negative energy balance and were catabolizing their own tissues. This was verified by a survey of the metabolic calculations, which disclosed that the average amount of body tissue catabolized was about 52 grams per square meter per day. From the mean weight loss found in this group, it appears that, for every 500 grams per square meter per day of weight lost, approximately one-tenth (50 grams per square meter per day) was due to catabolized body solids and the other nine-tenths represented water loss. This applies only to patients on a mixed oral diet and is entirely different from the 1:1 ratio found by Sturtz[9] for patients maintained completely by infusions of dextrose. A correlation of weight loss and the final daily balance divulged a relative similarity in trend; however, no mathematical formula that would be of practical value for accurately predicting the status of body fluid could be obtained.

Components of Water Metabolism.—Emphasis is placed on insensible water loss not only because it, along with metabolic water, is one of the two components of fluid balance that cannot be measured directly but because water of vaporization is little affected by available water and has preferential rights over the kidney.[24] The average of 642 ml. per square meter per day for insensible water loss by patients in our study was 65 per cent of that found by Heeley and Talbot[25] and was about 45 per cent greater than that reported by Newburgh and Johnston.[3, 18] Heeley and Talbot made their study on hospitalized children who had extremely high metabolic rates, while the Newburgh data were compiled on strictly basal, older patients. Emotional disturbances and physical activity apparently were the most influential factors governing insensible water loss in

our fourteen patients. None of our patients at any time exhibited severe oliguria, and there was no danger of water intoxication when the patients consumed fluids according to their own dictates.

The average daily urinary excretion of solutes (400 milliosmols per square meter) was well above the minimum of 200 applied by Talbot's[6] group and by Kerrigan and associates[7] to postoperative patients who were receiving enough water and carbohydrate to meet their needs. The patients apparently varied individually in their antidiuretic response to the emotional reaction, trauma, premedication, and anesthesia associated with total odontectomy. The over-all range in our series of patients was relatively close to the values in the twelve-hour to thirty-six-hour postoperative antidiuretic period found by Le Quesne and Lewis.[26]

The importance of the role played by emesis and surgical hemorrhage in upsetting the water equilibrium was exemplified by the average abnormal loss of fluid of almost 500 ml. per square meter on the first day. Visual estimations of blood loss in this type of operation are often surprisingly wrong, as was demonstrated by Gores.[10] It is feasible, then, that the body fluids should be replenished by the intravenous administration of solutions after severe surgical blood loss or postoperative vomiting. If nausea occurs postoperatively, intravenous infusions could help maintain the water equilibrium without "triggering" the vomiting reflex which so often is associated with oral intake during this time.

The average daily intake of water was near or more than 1,000 ml. per square meter on the first day except in three patients (Cases 3, 5, and 14, Table II); these three patients were in a gross negative water balance at this time. In light of the data presented in this study, the majority of patients recuperating from oral surgical procedures should be urged to drink more fluids. This general rule has been adhered to by most oral surgeons, but positive proof of its validity has not been offered.

The accuracy of the metabolic water value (160 ml. per square meter per day) calculated from these data could be questioned, since it was not certain that our patients were in the "steady state" that Newburgh's[3] group employed when they contrived this method. It was postulated from analysis of the metabolic mixtures that patients on an oral diet of carbohydrate, protein and fat catabolized less body tissue and thereby produced less metabolic water than did patients relying solely on carbohydrate. This theory is supported by the knowledge that the breaking-down of 1 gram of body protein produces 3.41 grams of water, of which 3.00 grams is preformed water.[3] Therefore, a value for daily metabolic water that is 110 ml. per square meter less than the value found in patients having only infusions of dextrose[2, 3, 9, 19] appears credible.

Water Balance.—As already noted, eleven of the fourteen patients were in a negative water balance on the first day and then changed to or toward a positive balance on the second day. Two of the remaining patients changed from practically a zero water balance on the first day to a mildly negative balance on the second day; this change in the first patient (Case 9) apparently resulted from a large reduction in fluid intake on the second day, and in the

second patient (Case 11) it was due to a threefold increase in urinary output after twenty-four hours. The remaining patient (Case 7) was in a barely positive balance on both days, with an increased urinary output on the second day being compensated by an increased fluid intake.

The inference is that most patients undergoing complete maxillary and mandibular odontectomy under general anesthesia are in a moderately negative water balance on the first postoperative day but are either in or on their way to a normal water balance on the second day. The only general pattern obvious from these eighty-four postoperative study periods of serum water concentration was that, as a group, the values were low, with sixty being at or below the physiologic minimum reported in the literature. Although these data coincided with the daily water balances, which were predominantly negative or near zero, no significant magnitude for the degree of dehydration could be ascertained from the values for serum water concentration. Numerous examples of conflicting comparisons could illustrate this point.[27]

Obligatory Water Loss and Daily Water Requirement.—It is obvious that the results of this study represent only mean values, and they will not enable one to predict the exact fluid status for any one patient. In an attempt to gain some reasonable estimation of the daily fluid requirement for patients after this particular operation, however, the daily obligatory water losses were utilized as a base. These losses include insensible water loss, obligatory urinary water, and abnormal losses. The metabolic water, which also is present at a constant rate in thirsting and fasting persons, can be subtracted from the obligatory losses to establish the relative daily water requirement. From the data found (Table II), the first day yielded a volume of 1,269 ml. per square meter, the second day yielded a value of 965, and the average for both days was 1,101. It is plausible that a figure of 1,250 ml. per square meter per day would be a representative value for the minimal water requirement for the first two or three days after operation for patients convalescing from oral surgical procedures.

SUMMARY AND CONCLUSIONS

A forty-eight-hour study of fluid balance was done on fourteen patients during and immediately after total odontectomy and alveoloplasty and while they were under the effects of general anesthesia. The body weight decreased daily in all but one of the patients. Eleven of the fourteen patients were in a negative fluid balance on the first day, and eight were in a slightly negative fluid balance on the second day. However, the classic signs of dehydration (dry and hot skin, dry tongue, sunken eyes, slight fever, and a urinary output insufficient to excrete normal waste materials) were not evident. No predictable correlation occurred betwen the serum water concentration and the actual findings of fluid balance.

Abnormal losses of fluid averaging 436 ml. per square meter of body surface during the first postoperative day stress the prominence of surgical blood loss and, to a lesser degree, of postanesthesia emesis as being the major cause

of water imbalance. Large abnormal losses or apathy toward fluid intake by the patient inevitably lead to a negative fluid balance. Postoperative intravenous infusions would be beneficial in averting this state.

From the findings on obligatory water loss, a minimal adequate intake of water was estimated to be 1,250 ml. per square meter of body surface per twenty-four hours. Most certainly, patients convalescing from oral surgical procedures should be urged to drink more fluids.

REFERENCES

1. Baird, E. E., and Stembridge, V. A.: Fluid and Electrolyte Imbalance: Limitations of Plasma Sodium Levels as a Measurement of Dehydration, Texas J. Med. **48:** 576-582, 1952.
2. Gamble, J. L.: Physiological Information Gained From Studies on the Life Raft Ration, Harvey Lect. **42:** 247-273, 1947.
3. Newburgh, L. H., Johnston, M. W., and Newburgh, J. D.: Some Fundamental Principles of Metabolism, ed. 2, Ann Arbor, Mich., 1945, J. W. Edwards.
4. Coller, F. A., and Maddock, W. G.: A Study of Dehydration in Humans, Ann. Surg. **102:** 947-960, 1935.
5. Talbot, N. B., Sobel, E. H., McArthur, J. W., and Crawford, J. D.: Functional Endocrinology From Birth Through Adolescence, Cambridge, Mass., 1952, Harvard University Press.
6. Talbot, N. B., Crawford, J. D., and Butler, A. M.: Homeostatic Limits to Safe Parenteral Fluid Therapy, New England J. Med. **248:** 1100-1108, 1953.
7. Kerrigan, G. A., Talbot, N. B., and Crawford, J. D.: Role of the Neurohypophyseal-Antidiuretic-Hormone-Renal System in Everyday Clinical Medicine, J. Clin. Endocrinol. **15:** 265-275, 1955.
8. Talbot, N. B., Kerrigan, G. A., Crawford, J. D., Cochran, W., and Terry, M.: Application of Homeostatic Principles to the Practice of Parenteral Fluid Therapy, New England J. Med. **252:** 856-862, 898-906, 1955.
9. Sturtz, G. S.: Water Metabolism After Cardiac Operations Involving Extracorporeal Circulation, Thesis, Graduate School, University of Minnesota, 1957.
10. Gores, R. J.: Blood Loss During Operation for Multiple Extractions and Alveoloplasty and Other Oral Surgery Procedures, Thesis, Graduate School, University of Minnesota, 1954.
11. Du Bois, D., and Du Bois, E. F.: A Formula to Estimate the Approximate Surface Area if Height and Weight Be Known, Arch. Int. Med. **17:** 863-871, 1916.
12. Sheard, C., and Sanford, A. H.: The Photelometer, Proc. Staff Meet. Mayo Clin. **8:** 516-518, 1933.
13. Sanford, A. H., Sheard, C., and Osterberg, A. E.: The Photelometer and Its Use in the Clinical Laboratory, Am. J. Clin. Path. **3:** 405-420, 1933.
14. Hall, R. E., and Sherrill, M. S.: Freezing-Point Lowerings of Aqueous Solutions. In Washburn, E. W.: International Critical Tables of Numerical Data, Physics, Chemistry and Technology, vol. 4, New York, 1928, McGraw-Hill Book Company, pp. 254-264.
15. Fiske Associates, Inc.: Fiske Osmometer Instruction Manual, 121 Liberty Street, Danvers, Mass. (Privately published.)
16. Crawford, J. D., and Nicosia, A. P.: A Method for the Determination of Freezing Point of Small Quantities of Biological Fluids, J. Lab. & Clin. Med. **40:** 907-913, 1952.
17. Newburgh, L. H., Wiley, F. H., and Lashmet, F. H.: A Method for the Determination of Heat Production Over Long Periods of Time, J. Clin. Invest. **10:** 703-721, 1931.
18. Newburgh, L. H., and Johnston, M. W.: The Insensible Loss of Water, Physiol. Rev. **22:** 1-18, 1942.
19. Butler, A. M., Talbot, N. B., MacLachlan, E. A., Appleton, J. E., and Linton, M. A.: Effect of Testosterone Propionate on Losses Incident to Inadequate Dietary Intake, J. Clin. Endocrinol. **5:** 327-336, 1945.
20. Wiley, F. H., and Newburgh, L. H.: An Improved Method for the Determination of Water Balance, J. Clin. Invest. **10:** 723-731, 1931.
21. Gamble, J. L., and Butler, A. M.: Measurement of Renal Water Requirement, Tr. A. Am. Physicians **58:** 157-161, 1944.
22. Barnett, H. L., Vesterdal, J., McNamara, H., and Lauson, H. D.: Renal Water Excretion in Premature Infants, J. Clin. Invest. **31:** 1069-1073, 1952.
23. Power, M. H.: Personal communication to the authors.

24. Maddock, W. G., and Coller, F. A.: Water Balance in Surgery, J. A. M. A. **108**: 1-6, 1937.
25. Heeley, A. M., and Talbot, N. B.: Insensible Water Losses per Day by Hospitalized Infants and Children, A. M. A. Am. J. Dis. Child. **90**: 251-255, 1955.
26. Le Quesne, L. P., and Lewis, A. A. G.: Postoperative Water and Sodium Retention, Lancet **1**: 153-158, 1953.
27. Bergan, R. D.: Fluid Balance After Operation for Multiple Dental Extractions and Alveoloplasty, Thesis, Graduate School, University of Minnesota, 1958.

PERIODONTICS

MICROSCOPIC STUDIES OF THE PERIODONTIUM OF THE ANTERIOR TEETH OF A 4-YEAR-OLD BOY

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INTRODUCTION

INVESTIGATIONS dealing with the microscopic changes in the periodontium of the human deciduous teeth during their functional period are scanty not only in number but also in detail. The few available reports deal mainly with the changes to the tooth proper as the result of developmental resorption[1, 5] or with traumatic injuries to the teeth in children of mixed dentition.[3, 4] For the most part, these studies were based on histologic sections of individual teeth obtained from children of varying ages. The difficulty in obtaining whole jaws and teeth from human subjects is probably the main contributory factor in the inadequacy of any study concerning the alterations to the periodontium of the deciduous teeth.

Because of the scarcity of available human material, it becomes of interest to describe in detail the morphologic features of the periodontium of the anterior teeth of a single 4-year-old boy when such material presents itself for study.

MATERIALS AND METHODS

This investigation is based on a study of the teeth and jaws of a 4-year-old boy whose body was donated to the Department of Anatomy, School of Medicine, University of Southern California, for scientific purposes. Both the mandible and the maxilla were perfused with a formol acetic acid-alcohol solution. The specimens were decalcified in 10 per cent nitric acid in 10 per cent formalin solution. The mandible and maxilla were then cut into blocks of tissue in such a manner that on one side the blocks of tissue contained one tooth, whereas on the opposing side the blocks of tissue contained two or three teeth. The specimens were dehydrated and infiltrated in the routine way for the nitrocellose-embedding method. The blocks of tissue were finally

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embedded in 50 per cent nitrocellulose, and the embedded blocks were sectioned in thicknesses of 20 to 25 micron. The cut sections were stained with hematoxylin and triosin.

OBSERVATIONS

Upper Central Incisor.—In a labiolingual section of the upper central incisor degenerative changes are observed (Fig. 1). The eruptive force exerted by the underlying developing permanent tooth has stimulated the resorption of the lingual alveolar bone so that only isolated spicules of bone remain. In addition, due to the lateral pressure produced by the labial movement of the permanent tooth, extensive bone loss to the labial alveolar bone also results. This destructive process has lowered the crest of the bone to the apical third of the root. Not only has the supporting bone been destroyed, but the pressure of eruption has extended into the tooth proper. This severe force has fragmented the apical portion of the root. Fig. 2 shows a high magnification of the apical area. Osteoclasts are seen adjacent to the labial dentine and cementum. The labial periodontal membrane, as well as the adjacent alveolar bone, exhibits histologic evidence of degeneration, such as edema, disorganization of the periodontal membrane, and lacunar resorption of the bone.

The gingivae of both the labial and lingual surfaces show mild inflammatory infiltration. Fig. 3 shows a section of the labial gingiva. The epithelial attachment has migrated apically alongside the cementum with rete pegs invading the adjacent connective tissue. Chronic inflammatory cells are present in both the epithelium and the connective tissue.

As the result of the severe destruction of the supporting bone and the accompanying loss of attachment fibers, the periodontium of the upper central

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Key to Abbreviations:

B = Bone.
C = Cementum.
Ca = Calculus.
D = Dentine.
E = Enamel.
E.A. = Epithelial attachment.
Ep. = Epithelium.
E.R. = Epithelial rests.
G = Gingiva.
I.C. = Inflammatory cells.
La = Labial surface.
Li = Lingual surface.
P.M. = Periodontal membrane.
Pu = Pulp.
Sc. = Supracrestal fibers of free gingival group.
T.F. = Transseptal fibers.

Fig. 1.—Labiolingual sections of the upper central incisor. Note the extensive bone loss on both the labial and lingual surfaces of the deciduous tooth and the splitting of the root. Observe the organization of the supracrestal fibers (Sc.). (Magnification, ×25; reduced ⅝.)

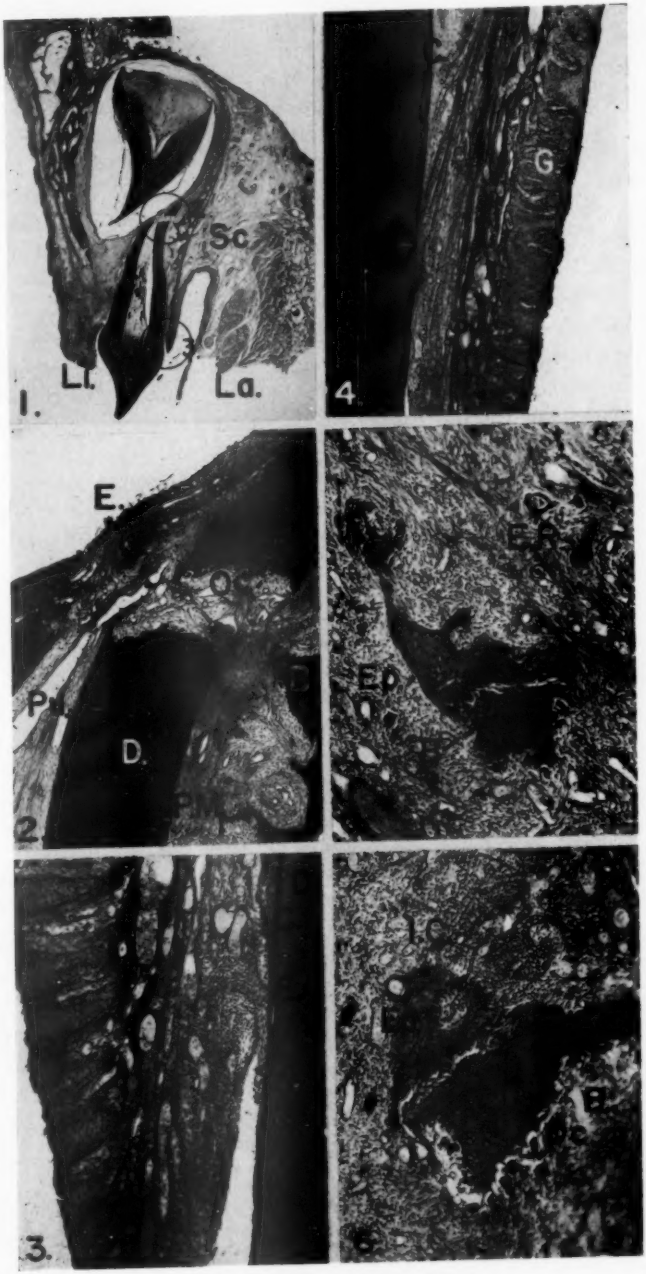
Fig. 2.—High magnification of area 2 of Fig. 1. Osteoclasts are located adjacent to cementum and dentine of the root fragments. Also observe the disorganization of the attachment fibers on the labial surface. (Magnification, ×250; reduced ⅝.)

Fig. 3.—Labial gingival section (area 3 of Fig. 1). The epithelial attachment has migrated apically on the cementum with rete pegs proliferating into the underlying connective tissue. Note the invasion of inflammatory cells in both the epithelium and the connective tissue. (Magnification, ×250; reduced ⅝.)

Fig. 4.—Upper third of the root of the upper central incisor. Note that the supracrestal fibers of the free gingival group have become thickened and organized to aid in the support of the tooth. (Magnification, ×150; reduced ⅝.)

Fig. 5.—High magnification of the lingual surface of the upper central incisor. Note the proliferation of epithelium derived from epithelial rests around the spicule of bone. (Magnification, ×250; reduced ⅝.)

Fig. 6.—High magnification of the lingual surface of the upper central incisor. In addition to the epithelial proliferation, there is an inflammatory infiltration. (Magnification, ×250; reduced ⅝.)



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incisor is considerably weakened. However, the supracrestal fibers of the free gingival group (*Sc*) have become thickened and highly organized as they pass from the cementoenamel junction to their attachment deep in the base of the maxilla (Fig. 1). Fig. 4 shows a high-magnification view of the origin of these fibers at the cementoenamel junction and their subsequent course apically in the tunica propria of the gingiva.

The fate of the lingual spicules of bone is demonstrated in Figs. 5 and 6. Fig. 5 shows a spicule of bone partially surrounded by proliferating epithelial cells originating from stimulated epithelial rests, whereas the opposing bony surface is lined with osteoclasts. The persistence of these spicules appears to stimulate an inflammatory reaction, as shown in Fig. 6.

Lower Central Incisor.—A labiolingual section of the lower central incisor is shown in Fig. 7. The eruptive force of the underlying permanent tooth has similarly produced extensive bony destruction to the lingual alveolar plate, so that only a thin shell of bone may be observed surrounding the crypt of the permanent tooth. The crest of the labial alveolar plate is still located at the upper third of the root. At the midpoint of the root, however, there is evidence of tooth-tipping characterized by the direct apposition of cementum to the alveolar bone. This direct contact between cementum and bone is evident in Fig. 8, which shows a high-magnification view of the midregion of the root.

The gingivae of both the labial and the lingual surfaces also show an inflammatory infiltration. Calculus is present in the crevice of the labial gingiva. The base of the epithelial attachment is located on the cementum. Both the epithelium and the underlying connective tissue are heavily infiltrated with chronic inflammatory cells (Fig. 9).

Lateral Incisors.—The changes to the periodontium of the upper and lower lateral incisors are similar in nature; thus, the microscopic features observed in the upper lateral incisor will be described. The eruptive force exerted by the permanent lateral incisor has not only destroyed the lingual bony plate but has extended into the adjacent periodontal membrane to produce severe degeneration to the connective tissue. The traumatic force resulting from the loss of support on the lingual periodontium and the labial movement of the permanent

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Fig. 7.—Labiolingual section of the lower central incisor. Note the tipping of the tooth as indicated by the direct apposition of the cementum to the bone. Also observe the thinning of the bony crypt of the underlying permanent tooth. (Magnification, ×25; reduced ⅝.)

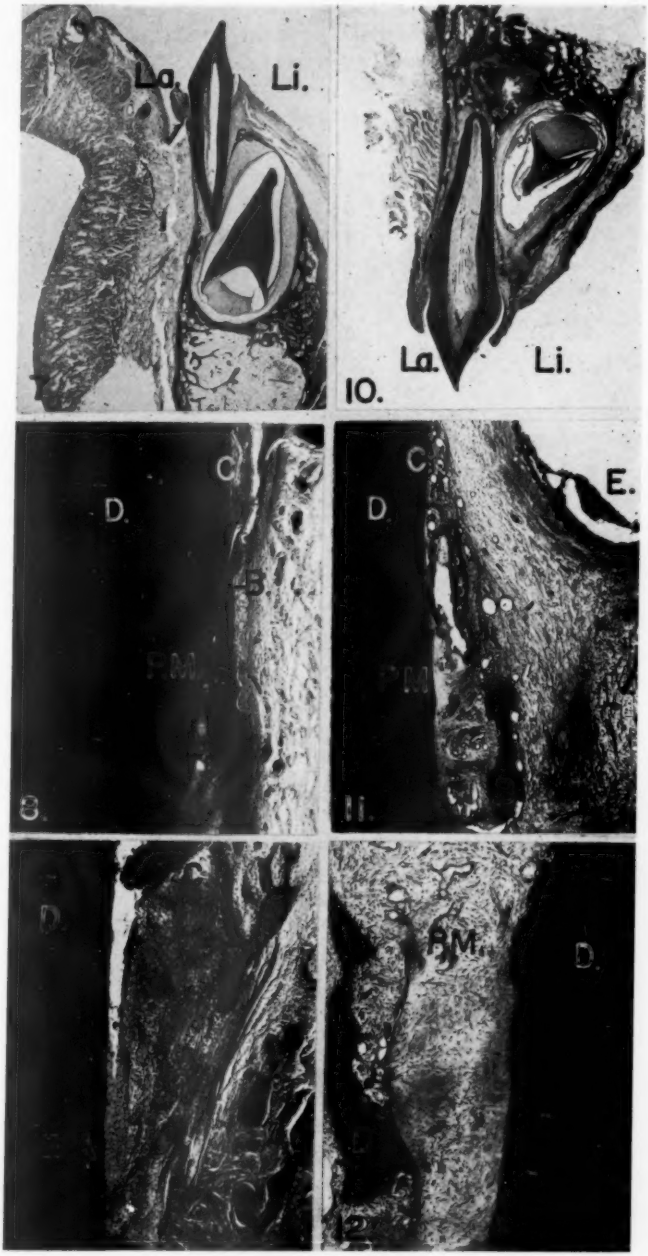
Fig. 8.—High magnification of the midroot region of the lower central incisor. Note the close proximity of the cementum to the bone, compressing the periodontal membrane. (Magnification, ×250; reduced ⅝.)

Fig. 9.—Labiogingival surface of the lower central incisor. Calculus is present in the crevicular area. Note the downgrowth of epithelial attachment upon the cementum and the inflammatory cell infiltration of both the epithelium and the subepithelial connective tissue. (Magnification, ×250; reduced ⅝.)

Fig. 10.—Labiolingual section of the upper lateral incisor. There is extensive destruction of the lingual periodontium with fragmentation of the bone. Note that the labial crest is still on the upper third of the root. (Magnification, ×25; reduced ⅝.)

Fig. 11.—High magnification of the lingual periodontal membrane. Note the tip of the cusp of the permanent tooth. The lingual bone has been destroyed, and the periodontal membrane shows necrosis, hemorrhagic areas, and loss of attachment fibers. (Magnification, ×250; reduced ⅝.)

Fig. 12.—High magnification of the labial apical region of the lateral incisor. Note the loss of attachment fibers, the presence of an edematous area, and osteoclasts associated with bone loss. (Magnification, ×250; reduced ⅝.)



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tooth has lowered the crest of the labial alveolar bone to the midroot region (Fig. 10). Fig. 11 illustrates the damage to the lingual periodontal membrane that occurs as the result of the severe eruptive force. The tip of the permanent lateral incisor (*E*) is in view. The periodontal membrane shows extensive necrosis, hemorrhage, and complete loss of attachment fibers.

Due to the weakening of the tooth support on the lingual aspect, degeneration to the apical region of the labial periodontal membrane is observed (Fig. 12). The membrane appears edematous, with complete loss of attachment fibers. In addition, lacunar resorption is noted in the adjacent bone.

The gingivae of both the labial and the lingual surfaces showed mild inflammatory involvement; however, the epithelial attachments were still limited to the cementoenamel junction.

Cuspids.—At this chronological age the periodontium of the upper and lower cuspids exhibited no extensive changes. In a labiolingual section of a lower cuspid, the crests of both the labial and lingual alveolar bone are found at the upper third of the root (Fig. 13). The only microscopic indication of bone resorption is restricted at the apical third of the lingual surface. The base of the epithelial attachments of both labial and lingual surfaces is limited to the cementoenamel junction (Fig. 14). The epithelium, as well as the underlying connective tissue, is free from inflammatory cells, and the attachment fibers are still intact.

Mesiodistal Sections.—In studying a mesiodistal section of the three upper anterior teeth, it is evident that the position of the underlying developing permanent teeth plays an indirect role in the weakening and destruction of the deciduous periodontium. Fig. 15 represents a mesiodistal section of the upper anterior teeth. The permanent central incisor is located directly apical to the deciduous central incisor, and because of its size its crypt expands distally toward the lateral incisor. As a result of the lateral extension of the permanent central incisor and the proximity of the maxillary sinus, the crypt of the permanent lateral incisor is located in the interseptal region between the lateral incisor and the cuspid. The permanent cuspid is not visible in this section, for its location is apical and mesial to the upper first premolar. Because of the position of the crypt of the permanent lateral incisor, the spongiosa of the interseptal bone is absent, with only a thin shell of the alveolar bone proper remaining.

The alveolar crests of the various interproximal regions are located at a higher root level than the crests of either the labial or the lingual alveolar plates. Fig. 16 illustrates the interproximal papillary region between the central and lateral incisors. The base of the epithelial attachment on both the mesial and the distal surfaces is limited to the cementoenamel junctions. The transseptal fibers appear to be intact. However, clefts are present in the gingival epithelium. The surface epithelium has proliferated into the underlying connective tissue. Keratinization has occurred in the center of the proliferating epithelial cells; as the keratin is sloughed off, a cleft results. Clefts are also noted in the lower gingivae.

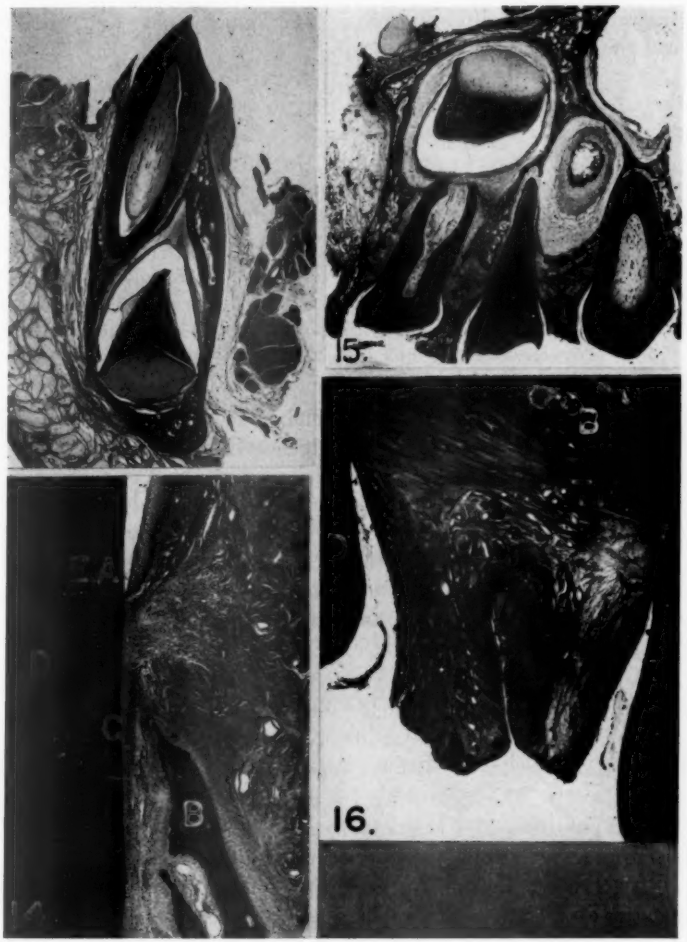

Fig. 13.—Labiolingual section of a lower cuspid. At this chronological age the only indication of bone loss is seen at the apical third of the lingual surface. Observe the crestal heights on both the labial and the lingual surfaces. (Magnification, ×25; reduced ⅜.)

Fig. 14.—High magnification of the lingual crestal area of the cuspid. The base of the epithelial attachment is limited to the cementoenamel junction. Note that the crest of the alveolar bone is just below the cementoenamel junction. (Magnification, ×250; reduced ⅜.)

Fig. 15.—Mesiodistal section of the upper anterior teeth. Note the position of the permanent central incisor and maxillary sinus. Also observe the crest of the interproximal bone and transseptal fibers. (Magnification, ×25; reduced ⅜.)

Fig. 16.—Interproximal gingiva. Note the gingival cleft. Note that the transseptal fibers are intact and that the crest of bone is still located in the upper third of the root. (Magnification, ×250; reduced ⅜.)

DISCUSSION

In the jaws of a 4-year-old boy, there are already present both intrinsic and extrinsic forces that alter the physiologic balance between functional occlusion and the supporting periodontium of the anterior teeth. The primary intrinsic force is the pressure produced by the erupting permanent teeth. Due to their position in relation to the deciduous teeth, loss of bone and disorganization of the periodontal membrane will first result on the lingual surfaces. The progressive destruction of the lingual periodontium is related to the stage of eruption of the permanent teeth. In the present study the cuspid teeth at the age of 4 years show no demonstrable alteration to the periodontium. With continued eruption, however, as seen in the lateral incisor, the eruptive force becomes so severe that it not only produces bone loss but causes necrosis and hemorrhagic areas in the periodontal membrane. In the central incisor the lingual periodontium of the deciduous tooth has been completely destroyed and has been replaced by a disorganized connective tissue.

Simultaneously, there is a labial movement of the permanent teeth which indirectly causes resorption of the labial alveolar plate, reducing the height of alveolar crest. The lowering of the alveolar crest, root resorption, and loss of attachment fibers on both the labial and lingual surfaces produces a change in the relationship of the clinical crown and root which will increase the extra-alveolar leverage on the teeth. This, together with excessive stress produced by the masticatory forces, creates secondary occlusal trauma and the resultant destruction becomes intensified, as seen in the upper central incisor.

With such an extensive loss to support on both the lingual and the labial surfaces, a question arises as to what factors enable such a tooth as the central incisor to remain in the jaw until physiologic exfoliation occurs between the ages of 6 and 7 years. It is apparent from the material studied that the supracrestal fibers of the free gingival group become organized into thick bundles that pass from the cementoenamel region toward the base of the maxilla, thus aiding in the retention of the tooth in the jaw. In addition, the supporting structures of the interproximal regions do not exhibit the same degree of destruction as the labial or lingual surface. The crest of the bone is still limited to the upper third of the root, and the epithelial attachment is located at the cementoenamel junction. The attachment fibers, especially the transseptal fibers, are intact.

In a previous report Bernick and Friedman[2] described gingival clefts in the interproximal gingiva of the deciduous anterior teeth of monkeys. In the present study clefts were also seen in the interproximal region of both upper and lower teeth. Their formation can be described as an extensive proliferation of the epithelium deep into the underlying connective tissue. Subsequently, the center of the epithelium becomes keratinized and later splits and sloughs off; thus, a cleft is formed.

Gingival disturbances in deciduous teeth have been reported in the literature. Massler, Schour, and Chapra[6] reviewed the literature concerning the incidence of gingival disturbances occurring in children, and they came to the conclusion that gingivitis was very frequent during the mixed-dentition stage. Berniek and Friedman[2] noted that in the deciduous teeth of monkeys the microscopic appearance of the gingivae varied from normal to that of a severe gingivitis with pocket formation. In the present investigation, gingival involvement depended upon the stage of physiologic resorption. The central incisors, both upper and lower, exhibited calculus and inflammatory infiltration. On the other hand, the cuspid teeth which show no signs of resorption exhibit no signs of gingivitis.

SUMMARY

1. The changes occurring in the periodontium of the anterior deciduous teeth of a 4-year-old boy were studied. The jaws and teeth were fixed in a formol acetic acid-alcohol solution, decalcified, dehydrated, and embedded in nitrocellulose in the usual manner.

2. As absorption of the deciduous anterior teeth progresses, the lingual alveolar bone undergoes extensive destruction, especially at the crestal region, lowering the latter and weakening the support; finally only spicules of bone remain.

3. At the beginning stages of shedding, the changes in the periodontal membrane are slight; however, they become intensified as the resorptive process continues. During the later stages secondary occlusal trauma is initiated, producing severe degenerative changes to the labial alveolar bone as well as to the periodontal membrane.

4. The microscopic appearance of the gingivae varied from normal to that of gingivitis. Calculus deposits were found in the anterior teeth.

5. Gingival clefts were noted in the interproximal areas of both the upper and lower jaws, and their development has been described.

6. The base of the epithelial attachment was found on the cementum in the anterior central incisors, whereas it was limited to the cementoenamel junction in the other anterior teeth.

REFERENCES

1. Bernick, S., Rabinowitch, B. Z., and Rutherford, L. A.: Microscopic Studies of the Teeth of a Six Year Old Boy; Tooth Absorption, Anat. Rec. **105**: 249, 1949.
2. Bernick, S., and Friedman, W.: Microscopic Studies of the Periodontium of the Primary Dentition of Monkeys. I. Anterior Teeth, ORAL SURG., ORAL MED. & ORAL PATH. **6**: 1239-1247, 1953.
3. Coolidge, E. D.: Traumatic and Functional Injuries Occurring in the Supporting Tissues of Human Teeth, J. Am. Dent. A. **25**: 343, 1938.
4. Gottlieb, B., and Orban, B.: Die Veranderungen der Gewebe bei übermassiger Beanspruchung der Zahne, Leipzig, 1931, Georg Thieme.
5. Kronfeld, R.: The Resorption of the Roots of Deciduous Teeth, Dental Cosmos **72**: 103, 1932.
6. Massler, M. I., Schour, I., and Chapra, B.: Occurrence of Gingivitis in Suburban Chicago School Children, J. Periodont. **211**: 146, 1950.

ORAL MEDICINE

ORAL MANIFESTATIONS OF BENIGN MUCOUS MEMBRANE PEMPHIGUS (MUCOUS MEMBRANE PEMPHIGOID)

Review of the Literature and Report of Fifteen Cases

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IN RECENT years insufficient attention has been directed to benign mucous membrane pemphigus as a distinct clinical entity, particularly in the differential diagnosis of vesiculating eruptions of the oral mucous membrane. Although the disease is relatively uncommon as compared to the incidence of pemphigus vulgaris, it is of considerable importance to the oral diagnostician, since it invariably involves the mucosa of the mouth. In many recent publications dealing with the oral lesions of pemphigus, insufficient differentiation is made between the various forms of pemphigus and pemphigoid eruptions. In recent years Lever[6-9] has offered significant contributions to an understanding of the nature and significance of the condition and has emphasized the importance of correct diagnosis. Lever[7] does not consider this interesting condition a form of true pemphigus, since the histopathology presents basic differences when compared to that of the more common varieties of pemphigus. True pemphigus is divided on the basis of clinical considerations, into four groups: pemphigus vulgaris malignus, pemphigus vegetans, pemphigus foliaceus, and pemphigus erythematosus (Senear-Usher disease).[7] Pemphigus vegetans is thought to be a variant of pemphigus vulgaris in which the patient reacts with increased resistance to the disease and in which vegetating hyperplastic lesions result.[3] Pemphigus erythematosus appears to represent an early phase or abortive form of pemphigus foliaceus or, in some cases, pemphigus vulgaris. Pemphigus-like diseases with a rather nonspecific microscopic picture are termed "pemphigoid" by Lever.[7] This group includes bullous pemphigoid and benign mucous membrane pemphigus or pemphigus conjunctivae.

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Because of its clinical manifestations, benign mucous membrane pemphigus has been regarded in the past as a particular form of pemphigus. The histologic studies by Lever[7, 8] indicate that this condition does not belong in the pemphigus group proper and suggest that the term "benign mucous membrane pemphigoid" would be more accurate. In a recent study,[12] we have confirmed Lever's observations. Continued studies are indicated before the basic nature of this condition can be understood and its significance fully appreciated.

HISTORICAL REVIEW

Benign mucous membrane pemphigus was apparently first described by Wichmanns[19, 20] in the late eighteenth century. He described a female patient who had ocular and oral involvement as well as skin lesions. The duration of the disorder was three years, and the entire oral cavity appeared denuded of epidermis. Thost,[16-18] in 1896 and in subsequent papers, distinguished between an "acute pemphigus of mucous membranes" usually seen in pemphigus vulgaris, foliaceus, and vegetans and a "chronic pemphigus of the mucous membrane." To Thost we owe the first detailed description of the disease as well as the original nomenclature. In 1896 he evaluated a series of cases from the literature and discussed two cases seen by himself. The rarity of the disease was emphasized, and it was pointed out that, because of the serious ocular adhesions, most cases were seen by ophthalmologists. The oral symptoms were noted but were not considered serious. In 1911 Thost used the term "mucous membrane pemphigus" and listed its salient features as follows:

"1) Exclusive participation of the mucous membrane and total freedom on the part of the skin surface, with only very exceptional extension of the mucous membrane to directly adjacent skin areas.

"2) Very regular participation of the connective tissue of the eye which leads to essential shrinking thereof and later to Phthisis bulbi.

"3) There is always a tendency for the growing together of adjacent parts of the mucous membrane and for shrinkage of deeper structures of the mucous membrane.

"4) A chronic feverless course.

"5) Concurrent general cachexia and poor nutrition of the skin and poor development of the muscles.

"6) Completely unaffected by medication, especially iodine and mercury. Wassermann negative."

In summary, Thost indicated: "There are, in short, completely different diseases of the skin and mucous membrane which have in common the symptom of blister formation in the upper strata. The cases of chronic mucous membrane pemphigus are distinguished from the many forms of pemphigus (Martius alone counts 97 different varieties) by a very particular course. They represent in all cases a very definite and in all cases an identical disease pattern which is sharply characterized by its course and its localization."

Early descriptions of cases of benign mucous membrane pemphigus with conjunctival and other mucosal lesion were offered by Morris and Roberts[13] and Nettleship.[14]

CLINICAL APPEARANCE AND COURSE

The disease usually runs a rather benign, chronic course. The patient's general health is not significantly affected, and fatal cases are extremely rare. The mucous membranes, particularly the conjunctivae and the mucosa of the oral cavity, are characteristically involved, and the vesicular lesions tend to result in scarring, although this complication is not common in relation to the oral lesions. In benign mucous membrane pemphigus, the mucous membranes are always affected and the skin is involved in approximately 50 per cent of the cases. The scarring invariably occurs as a result of the conjunctival lesions, with partial or total blindness as the serious outcome. Scarring may also occur on skin and on other mucosal surfaces, although the oral tissues are spared this complication. The disease runs a protracted course with periods of exacerbation and remission. It may become relatively inactive after a long course of activity.

Although the early reports by Thost[16] stress the extreme rarity of the condition, it appears to be more common than previously supposed. Of 153 cases of pemphigus and pemphigoid discussed by Lever,[7] thirty cases of benign mucous membrane pemphigus are listed. In these thirty cases, twenty-seven patients presented oral lesions, with some scarring occurring in five instances. Twenty-four of the patients presented conjunctival involvement, with scarring in all cases and blindness in eight. The mucosa of the throat was involved in fourteen cases, the esophagus in four, the nasal mucosa in twelve, the anal mucosa in one, the genital mucosa in eight, and the skin in thirteen cases. In eight cases the initial lesion appeared in the oral cavity, while in eleven cases the eyes were the primary site of involvement.

Lever found the age at onset of lesions to vary from 30 to 84, with an average age of 60. There were eleven male patients and nineteen female patients in Lever's series. Both of Thost's patients were men. Unlike pemphigus vulgaris, which involves a high percentage of Jews, benign mucous membrane pemphigus is not commonly seen in patients of Jewish extraction. Only one of the thirty patients in Lever's series was Jewish, in distinction to the relatively high figures for pemphigus vulgaris.

The etiology of the condition is not known at present. It is hoped that as more cases are reported and newer diagnostic procedures utilized, perhaps some understanding of this interesting disease will be gained. The condition is of particular importance to the dentist, since the oral cavity is very often involved and the gingival mucosa is usually characterized by a desquamative type of gingivitis. The oral involvement may often be the initial sign of the disease process and may be confused with several other diseases presenting somewhat similar vesiculations of the oral mucosa.

We have reported recently on fifteen cases of benign mucous membrane pemphigus seen by us in private practice, in consultation, and in the Oral Medicine Clinic of Tufts University School of Dental Medicine.[12] In the present report we shall discuss the oral manifestations in more detail. It is of interest that in our series oral lesions were present in all fifteen cases and these lesions first caused the patients to present themselves for diagnosis and therapy. None of our fifteen patients was Jewish. Nine of the patients were women and six were men. The age at onset of lesions varied from 23 to 75. The duration of the lesions ranged from several months to thirty years in one case.*

SKIN LESIONS

Skin lesions were present in only 20 per cent of our cases, which is in contrast to a higher incidence reported in the literature. Perhaps this is due to early therapy in many of our cases.

When skin lesions are present, the face and scalp are the most commonly involved areas. There is nothing characteristic from a clinical standpoint. Pathologically, a subepidermal bulla is observed without evidence of acantholysis. This is similar to bullous erythema multiforme, but true pemphigus can be ruled out. The associated mucous membrane lesions are necessary for a definite diagnosis. Their appearance and subsequent healing usually follow mucous membrane activity.

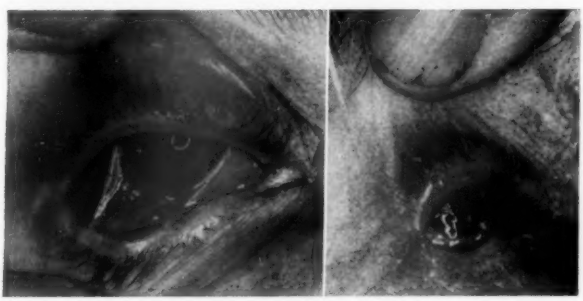

Fig. 1.—Ocular involvement in benign mucous membrane pemphigus. Early involvement with symblepharon (left) and late involvement with severe scarring and blindness (right).

OCULAR LESIONS

The conjunctivae frequently are involved, and this is responsible for the terms "ocular pemphigus" and "pemphigus conjunctivae." One should always look for evidence of their involvement, as this manifestation can be of definite value in establishing the diagnosis.

*We are greatly indebted to Professor Francis P. McCarthy for his interest and encouragement and for his help in making available to us the records of several cases that he had followed for many years before we had occasion to study them.

Eye lesions represent the most serious complication, as considerable loss of vision may result from the scarring (Fig. 1). Ophthalmologic consultation should be obtained in all cases, even if there is no obvious eye involvement.

ORAL LESIONS

The oral mucosa was involved in all of our cases and is rarely, if ever, spared in any case. There are several features that help to differentiate this disease from other bullous eruptions. The lesions usually develop slowly, with only one or two areas of involvement early in the disease (Fig. 2). Very often weeks pass before further lesions are observed. This is in contrast to pemphigus vulgaris and erythema multiforme, in which widespread involvement may occur in a matter of twenty-four to forty-eight hours. The individual lesions are usually smaller, although coalescence may take place. The extensive peripheral

Fig. 2.—Early involvement of oral mucosa in benign mucous membrane pemphigus. Note the single vesicle on the mandibular gingiva in relation to the premolar.

enlargement seen in pemphigus vulgaris is absent. If the patient is dentulous, the gingivae are the most common site of involvement in our experience (Figs. 3 to 5). Many of these patients are treated for desquamative gingivitis and other conditions in the early stages of the disease. Fresh vesicles and bullae are rarely observed, but a recently collapsed bulla presents a fairly characteristic lesion with the thick white epithelium partially denuded and resting on a bright, erythematous, eroded base (Figs. 6 to 8). This is in contrast to pemphigus vulgaris, in which the epithelium is thinner, friable, and easily detached (Fig. 9). Fairly diffuse erythema and edema of the gingivae, with occasional vesicle or bulla formation, are not uncommon. The various stages of development and healing are slower than other bullous diseases, and scarring may be observed. This is rare in the oral cavity as opposed to the conjunc-

tissue and may involve the mucobuccal folds and the posterior aspect of the oral cavity about the uvula and tonsillar area. Despite these criteria, considerable difficulty in diagnosis may exist, and histologic examination should be performed to add further evidence.

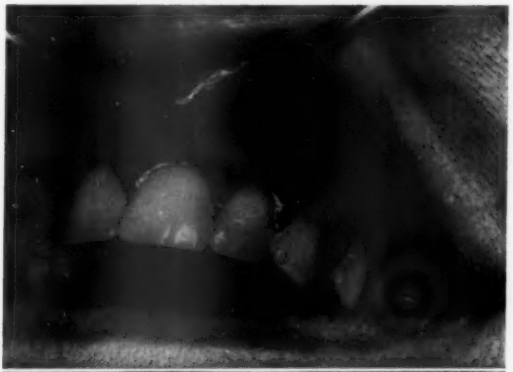

Fig. 3.

Fig. 4.

Fig. 5.

Fig. 3.—Diffuse erythema of the attached and marginal gingiva with patchy areas of desquamation. The color is a bright red with some whitish areas. Benign mucous membrane pemphigus.

Fig. 4.—Intense diffuse reddening of gingiva with some enlargement and edema in a case of benign mucous membrane pemphigus.

Fig. 5.—Patchy erythema of attached and marginal gingiva. This photograph was taken during a relatively quiescent stage of the disease.

Fig. 6.—Collapsed bulla on mandibular gingiva.

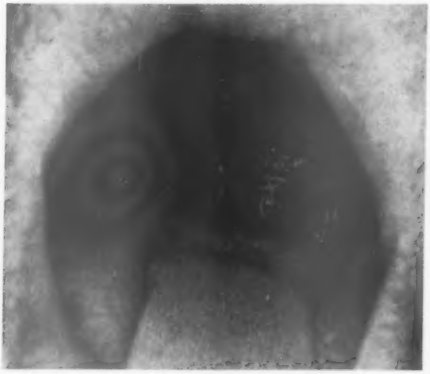

Fig. 7.—Collapsed bullae on hard palate, soft palate, and uvula.

Fig. 8.—Large bulla on edentulous maxillary ridge and numerous vesicles on buccal mucosa. Note the thickness of the vesicles and bulla and the intense erythema surrounding them.

DIFFERENTIAL DIAGNOSIS

Pemphigus Vulgaris.—This disease is much more rapid in its development and is often fatal in a few months if it goes untreated. The bullae are thin-walled and transient, leaving large eroded areas. The entire oral mucous membrane rapidly becomes involved, and maintaining proper nutrition becomes a major problem. Large areas of skin present bullae, and conjunctival lesions are rare. The histologic evidence of acantholysis is diagnostic (Figs. 9 and 15).

Erythema Multiforme Bullosa.—This is an acute inflammatory disease characterized by involvement of mucous membrane and/or skin with vesicles and bullae (Fig. 10). The patients often are constitutionally ill, and the disease runs a definite course with eventual clearing of all manifestations. Some etiology, such as a drug sensitivity, focus of infection, or emotional disturbance, may be evident. One should look for the classic target lesions of the skin, which are diagnostic.

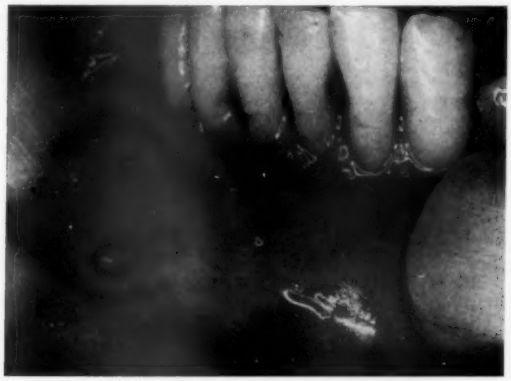

Fig. 9.—Pemphigus vulgaris. Note the collapsed, thin-walled bullae and vesicles on the labial mucosa.

Bullous Pemphigoid.—This is a rare, chronic, and relatively benign eruption which in the past has been referred to as chronic pemphigus. It is most commonly observed in the elderly and, if untreated, may contribute to the patient's death. The histologic picture is nonspecific, showing a subepithelial bulla like that seen in cases of benign mucous membrane pemphigus. The lesions consist of bullae which are widespread over the skin but which often spare the oral cavity.

Bullous Lichen Planus.—This is a rare form of lichen planus which, in some cases, is extremely difficult to differentiate from benign mucous membrane pemphigus (Fig. 11). The development of new lesions is slow, the course is prolonged, and constitutional symptoms are absent. Lichen planus, however, does not involve the eye. There may be skin lesions which will help to confirm the diagnosis. Close observation of the oral lesions discloses infiltration

about the erosions, and striae are usually present. In lichen planus a peculiar violaceous color is also quite characteristic. The pathologic findings are usually diagnostic in lichen planus.

Fig. 10.

Fig. 11.

Fig. 10.—Erythema multiforme. Note the coated tongue often seen in febrile diseases, the bulla and vesicles on the tip and lateral margins of the tongue, and the crusting on the lower lip.

Fig. 11.—Bullous lichen planus. Note the ulcerated area on the dorsum of the tongue, resulting from rupture of a bulla. Above the ulcerated area are the white striations typical of lichen planus.

Virus Diseases.—Acute herpetic gingivostomatitis and herpangina are acute infectious diseases characterized by constitutional symptoms, a sudden onset, and a short course. The lesions are generally confined to the oral cavity and are small, vesicular, and quite uniform.

Muco-ocular Syndromes.—Behçet's and Reiter's diseases may have both oral and eye lesions which can mimic some of the symptoms of benign mucous membrane pemphigus. The lesions are erosive rather than bullous, however,

and they do not present the gingival reaction and widespread oral or facial involvement. Furthermore, genital lesions are essential to fulfill the criteria for these diseases.

Desquamative Gingivitis (Gingivosis).—The etiology of this condition is obscure, and there is considerable doubt as to whether it is, indeed, a specific entity or merely a nonspecific gingival manifestation of a variety of systemic disturbances. Hormonal factors have been implicated, and a desquamative gingivitis occasionally follows hysterectomy and oophorectomy in young women. Clinically, desquamative gingivitis is seen as a diffuse erythema of the marginal and attached gingiva with areas of desquamation and occasional vesicle formation. Clinically and microscopically, the lesions of desquamative gingivitis are similar to the gingival lesions of benign mucous membrane pemphigus, but involvement other than gingival is extremely uncommon in the former condition. We are at present inclined to consider desquamative gingivitis as a manifestation of various disorders, and we feel that it is commonly a feature of benign mucous membrane pemphigus. Often the desquamative type of gingivitis is the initial manifestation of mucous membrane pemphigus, and correct diagnosis at this time may prevent prolonged ineffective therapy.

Aphthous Stomatitis.—This condition consists of a recurrent pattern of single or multiple, sharply demarcated ulcerations with marginal erythema. Etiology is unknown, but a psychosomatic relationship has been considered a possibility in recent years. Involvement is confined to the oral cavity.

MICROSCOPIC FEATURES

Tissue from oral lesions in several cases of benign mucous membrane pemphigus was studied microscopically. In one case we were fortunate in being able to obtain a biopsy specimen of an intact vesicle. Other biopsy specimens were taken of ulcerated areas and of gingival involvement characterized by desquamation. When an intact bulla is studied, microscopic examination reveals a definite, clear-cut subepithelial vesicle. A split is seen at the epithelium-connective tissue margin. The basement membrane appears to undergo destruction. The entire layer of stratified squamous epithelium is lifted off from the lamina propria of the connective tissue (Fig. 12). This is markedly different from the usual pattern in pemphigus vulgaris in which the bulla is intraepithelial and the epithelium splits above the stratum germinativum. Numerous cells lie free in the vesicle, and the acantholysis is a characteristic feature of pemphigus vulgaris (Fig. 15). In benign mucous membrane pemphigus acantholysis is not noted, and the vesicle itself contains clear fluid with scattered polymorphonuclear leukocytes, lymphocytes, histiocytes, and eosinophils. The connective tissue at the base of the vesicle is very densely infiltrated with polymorphonuclear leukocytes and chronic inflammatory cells as well as scattered eosinophils. The vesicle fluid stains lightly eosinophil, suggestive of mucoid material.

Studies from desquamating areas reveal stratified squamous epithelium undergoing degeneration. The underlying connective tissue is densely infiltrated

with lymphocytes, plasma cells, polymorphonuclear leukocytes, and histiocytes. The polymorphonuclear leukocytes are rather dense close to the surface. In some areas a definite split or separation is noted between epithelium and the underlying lamina propria (Fig. 13).

Fig. 12.

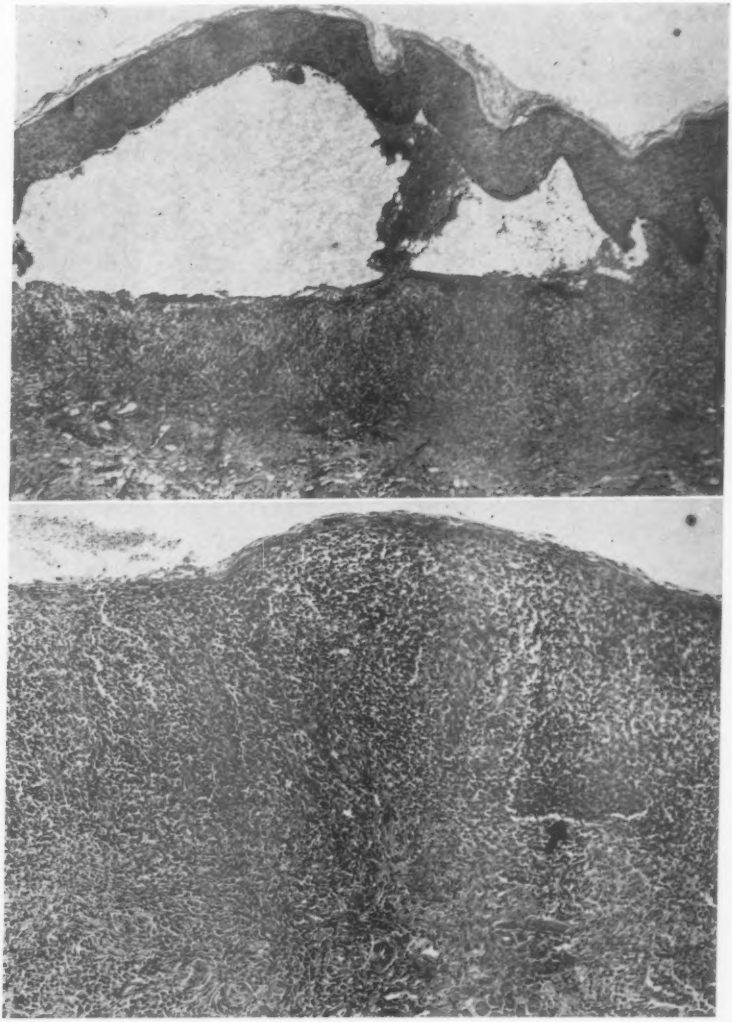

Fig. 13.

Fig. 12.—Low-power study of a vesicle in benign mucous membrane pemphigus. Note the entire epithelium lifted off from the underlying connective tissue and a dense inflammatory infiltrate at the base of the vesicle. The vesicle itself contains clear fluid and scattered polymorphonuclear leukocytes and lymphocytes.

Fig. 13.—Low-power study of a gingival biopsy specimen in benign mucous membrane pemphigus. Note the degeneration of the epithelium and the dense inflammatory infiltrate. In several areas there is a definite split between epithelium and lamina propria (arrow).

Biopsies of gingival lesions reveal a thin degenerating epithelium and a dense infiltrate of polymorphonuclear leukocytes and chronic inflammatory cells in the underlying connective tissue (Fig. 14). In summary, these microscopic findings present a nonspecific picture of epithelial degeneration, ulceration,

Fig. 14.

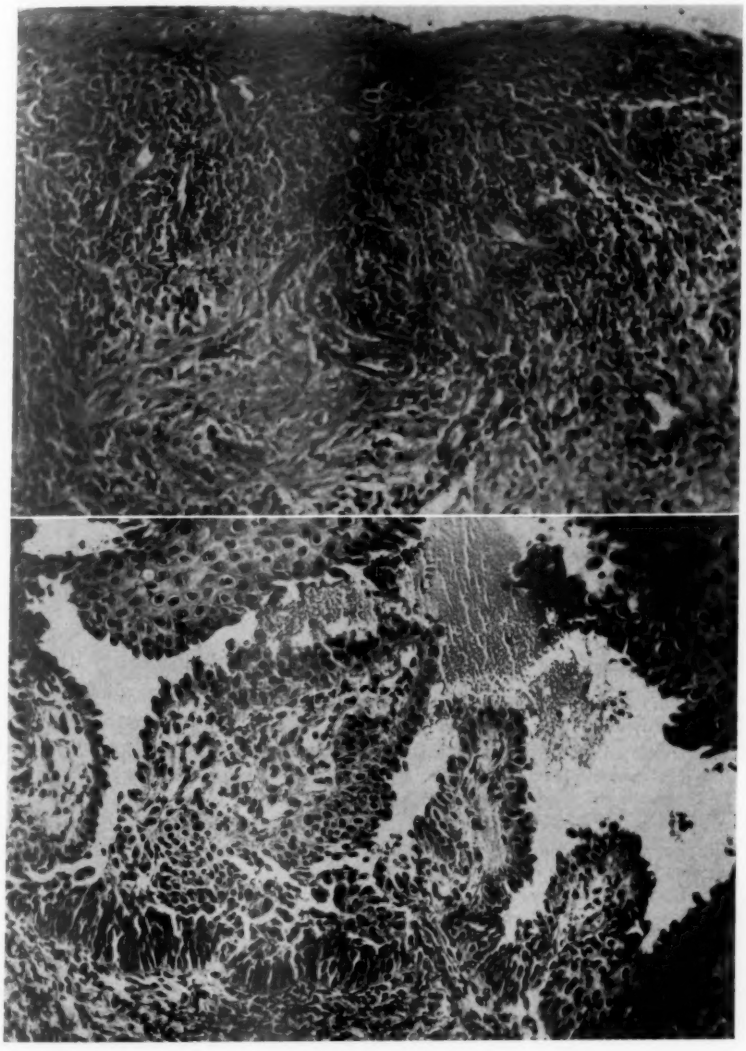

Fig. 15.

Fig. 14.—High-power study of a gingival biopsy specimen. Note the thin, degenerating epithelium and the intense inflammatory reaction in the underlying connective tissue.

Fig. 15.—High-power study of a bulla in pemphigus vulgaris. Note the intraepithelial splitting with acantholysis. The split is noted in the stratum spinosum close to the stratum germinativum.

subepithelial vesicle formation, and chronic inflammation. The subepithelial vesicle is preceded in the earlier stages by a well-defined cleft between epithelium and connective tissue. The suggestion may be made that disintegration of basement membrane may in some way be related to this type of lesion. However, this again is a relatively nonspecific finding in inflammatory lesions. The absence of acantholysis would distinguish these lesions from pemphigus vulgaris. In the latter disease, a diagnosis may be made on histopathologic examination, even when the clinical picture is indefinite and only a single lesion is present (Fig. 15).

THERAPY

There is no specific treatment for benign mucous membrane pemphigus. With the introduction of the corticosteroid hormones, however, complete or partial suppression of the manifestations of the disease is possible (Fig. 12). Successful management of these cases is usually not entirely in the realm of the dental profession, and these patients should be under the care of a qualified physician. However, the dentist can be of considerable help to the patient from a local standpoint. Proper care of teeth and gingivae is essential to keep local inflammation at a minimum. Since the gingivae are usually involved, periodontal treatment is mandatory. When prostheses are present, they must fit properly, as the least instability can produce considerable denudation of epithelium.

Topical medication is often helpful, and this includes regular lavage with soothing washes to reduce tissue inflammation. The success of the local application of corticosteroids is unpredictable. Frequent application on a relatively dry field has produced the best results in our experience with these medications. They should be gently massaged into the inflamed area with the finger tip.

Pain is usually a troublesome symptom and may discourage the patient from maintaining proper nutrition. The application of topical anesthetic agents before meals is advised in order that the patient might partake of a more varied selection of food. We have found dyclonine to be both safe and effective.

CASE REPORTS

The three case reports that follow are typical of the various aspects of this condition.

CASE 1.—Patient A. S., a 57-year-old woman, was first seen in 1938 with a complaint of "sore mouth," more or less confined to the gingiva for a period of three years. The oral condition followed an injury of the lower back (fractured coccyx) in 1935. Five weeks after the injury the patient developed blisters on the maxillary and mandibular gingivae and occasional lesions in the throat. The subjective symptoms were characterized by pain and tenseness in the gingivae. The blisters were large and flaccid, with colorless fluid contents. Associated with the oral lesions for two years (1936 to 1938) there was blister formation of both eyes, and the patient was treated in hospital A. In 1941 she was examined at hospital B, and the condition was diagnosed at this time as chronic aphthous stomatitis.

The patient was next seen in 1949. She was taking thyroid extract, 2 to 5 grains daily. There was no appreciable change in the oral condition. There was, at this time, a bullous lesion on one finger as well as a somewhat similar lesion on the chest. These lesions cleared after a few weeks. Lesions on the eyeballs had appeared two or three times a year for the past ten years. In 1949 the right breast was removed following a diagnosis of adenocarcinoma. From 1949 to 1951 the patient was under therapy at hospital C, without significant improvement and without change in the general course of the disease.

In November, 1951, bullous lesions of the gingiva were more numerous and lesions were present on the cornea of both eyeballs. The patient was taking Aureomycin, 250 mg. daily. Cortisone eye drops were used for the first time in 1951, with some results. In January, 1952, the nostrils were involved and associated with occasional nosebleeds. Vesiculation and crusting were noted. In April, 1952, there was an exacerbation of the oral lesions following the death of the patient's mother. During 1953 there was marked involvement of the gingiva, with the formation of bullae. Lesions also formed on the palpebral conjunctiva of the left eye. The patient refused to use cortisone at this time. She weighed 150 pounds, about 20 pounds less than her normal weight, and complained of a sore nose and throat.

In April, 1954, new lesions were seen on the vulva and vaginal mucosa. These lesions were bullous in character.

In October, 1954, the patient had been taking hydrocortone, 120 mg. daily, for three months with an improvement of the lesions. She stopped therapy, and there was a flare-up in the lesions of mouth, palate, and tonsillar region. Activity in the nares and vaginal involvement also followed the discontinuation of the drug. The patient's arthritis improved while she was taking cortisone.

When seen in December, 1954, the patient was taking hydrocortisone, 20 mg. four times daily to be gradually reduced to 20 mg. twice daily.

In April, 1955, there had been marked improvement for several months. The gingiva showed mild involvement. No ocular or vaginal lesions were present at this time. The patient took hydrocortisone, 20 to 40 mg., for recurrence of gingival bullae and the lesions promptly aborted. There was no eye involvement for several years. Her general health was improved, but she complained of having little strength and suffered from chronic fatigue. There was some activity in the nares with nosebleed. The lesions were cauterized by an otolaryngologist. In May, 1955, there was involvement of the palpebral conjunctivae of both eyes. This subsided promptly following the use of 20 mg. hydrocortisone three times daily.

In October, 1955, there was a vesicle on the right middle finger. The patient was taking hydrocortisone, 20 mg. three times daily.

In May, 1956, she had taken no cortisone for four months and the gingiva showed little activity.

In February, 1957, the patient was treated at hospital D for rheumatoid arthritis and anemia. She was given iron and liver injections with good results. Mouth lesions were not active, and there was only slight erythema of the gingivae. Her weight was 174 pounds, and her general condition was good. She had taken no cortisone since January, 1956. Blood studies were normal.

When the patient was seen in August, 1957, benign mucous membrane pemphigus had been active for one week, with lesions on the gingivae, nares, and right middle finger. The patient used meticortone, 5 mg. three times daily, with prompt improvement of all signs and symptoms.

In January, 1958, the patient gave up her work as a clerk and retired on a pension. She did well until October, 1957, when she contracted influenza followed by a flare-up of the gingivae and throat. Self-medication by the patient included 30 mg. hydrocortone daily. The patient was now working part time in a store.

In March, 1958, there was renewed activity. The gingivae were very sore (Fig. 4) and presented marked swelling and erythema. Bullae were present on the buccal mucosa. Prednisone, 40 mg. daily, was prescribed and was followed by improvement.

In June, 1958, marked improvement was noted. The disease was not active, and the patient was taking a sustaining dose of prednisone, 5 mg. daily.

In summary, this 58-year-old woman has been under treatment since 1938 for benign mucous membrane pemphigus which began in 1934. Since 1951 she has been treated with various preparations of cortisone. This treatment has been effective in controlling the various flare-ups which have occurred since 1951.

Prior to 1951 the disease was not effectively controlled with the various treatments used, but the patient felt that Aureomycin therapy gave her some relief. The patient continued to work almost continuously from 1934 until she retired in 1957. She is now doing part-time work, and at present (June, 1958) her general condition is good with no activity of the oral, eye, or skin lesions.

CASE 2.—The patient was M. A. H., a 65-year-old woman. Her first visit was in September, 1951, when her chief complaint consisted of sore gums and soreness of the mouth and deep into the throat. This condition first appeared three months prior to her first visit. She was treated with Aureomycin by a private physician and referred for study to hospital A. Laboratory findings were helpful in making a diagnosis.

Examination of the oral cavity showed marked erythema of the gingivae (generalized), which were rather tense and tender. No bullae were demonstrated on the initial visit. There was an eroded area on the left soft palate. The patient complained of a raw feeling in the throat, sore gums, and tracheal irritation. Treatment consisted of hydrocortone, 150 mg. daily. In October, 1951, a bullous lesion was demonstrated on the gingiva in the right upper central incisor region. The lower left second molar was extracted (mandibular infection).

In November, 1951, a large bullous lesion developed in the left tonsillar region. Blood examination was within normal limits.

In January, 1952, the patient had a bronchial cough with profuse expectoration of mucus.

In March, 1952, she was taking 60 mg. hydrocortisone daily. There was a bullous eruption on gingiva and left palate.

In April, 1952, the condition was still active. Hydrocortisone was increased to 150 mg. daily.

In July, 1952, the patient was taking four to six 20 mg. tablets of hydrocortisone daily. This seemed to control the activity of the oral condition.

In September, 1952, the condition was much better. A sustaining dose of 100 mg. of hydrocortisone daily was prescribed.

In January, 1953, the patient was putting on weight. She averaged 80 mg. hydrocortisone daily. The right upper central incisor was removed.

When the patient was seen in June, 1953, she was under nervous strain. Her son was sick with rheumatic fever. There was no great change in her condition.

In November, 1954, the patient was on vacation in Europe. Her condition was much improved for one month without cortisone. The gingivae showed no edema and erythema and no bullae.

In February, 1954, the patient was better. There was a small bulla on the palate. The patient was in good general condition.

In May, 1954, she was very nervous, as her son was to have a heart operation. There was a flare-up in the tonsillar region and palate. Hydrocortisone was increased to 120 mg. daily.

In February, 1955, she had done well on 40 to 60 mg. hydrocortisone daily with intervals where no cortisone was taken up to one month.

In January, 1956, she was holding very well. There was only slight gingival involvement. The patient was taking prednisolone, 15 to 20 mg. daily.

In July, 1957, she had had no "blisters" for two years on the gingiva. She had had only one skin lesion, three years ago on the forehead; the blister lasted for two weeks. She

was now using prednisone, 5 mg. twice daily, and skipping the use of cortisone for one week every six weeks. Her general health was good.

In September, 1957, the patient died suddenly of coronary heart disease at the age of 65 years.

In summary, this was a rather severe form of benign mucous membrane pemphigus, beginning at the age of 59 years and lasting until the patient's death at 65 years of age. The gingiva presented characteristic lesions throughout, with lesions elsewhere in the oral cavity. There was a question of tracheal involvement in the beginning of the disease. Rather large doses of cortisone were necessary to control the disease. A single bullous skin lesion occurred on the forearm early in the course of the disease. The condition was quiescent but not cleared up at time of death from coronary heart disease.

CASE 3.—The patient was J. B. A., a 75-year-old man. He first experienced difficulty with his oral cavity in 1953. He described his trouble as a "sore mouth" due to wearing artificial dentures. In 1954 he obtained a new set of dentures and noticed some relief. He continued to have erosions of his oral cavity but did not seek medical advice. In the spring of 1950 he noticed some inflammation of the left eye. He was seen by an ophthalmologist who gave him some local therapy. At this time his oral mucous membrane was markedly involved and he was referred to one of us (P. L. M.) for evaluation.

At the time of the first examination in July, 1956, the patient showed numerous erosive areas of the oral cavity, most marked in the pharyngeal area (Fig. 7). The patient was wearing full upper and lower dentures, and some inflammation was seen at several sites beneath the dentures. There was an early symblepharon of the left eye. A diagnosis of benign mucous membrane pemphigus was made. The patient was given prednisolone, 25.0 mg. daily, as well as dyclonine for topical application. In August, 1956, his condition had improved, and the prednisolone dose was lowered to 15.0 mg. daily. He continued to show slow but definite improvement. Meanwhile, he was hospitalized and lysis of his ocular adhesions was performed. In November, 1956, the dose of prednisolone was reduced to 10.0 mg. daily. Finally, after gradual reduction, he has been maintained on 5.0 mg. daily since February, 1957. His oral lesions continued to improve and, when seen in January, 1958, he was entirely clear. He still showed minimal conjunctival inflammation, and it was decided to continue with his present dosage. When last seen, he continued to remain free of any disease activity.

SUMMARY OF CASE REPORTS

The three case reports present several typical features that frequently are encountered in cases of benign mucous membrane pemphigus. The first two cases demonstrate the chronicity of the disease and its recalcitrant nature to all forms of therapy except corticosteriods. The benign nature of the entity is indicated by the duration of the disease without serious effect on the general health of the patient. It is very interesting to note how long the patients were studied before a correct diagnosis was established. The third case, although very extensive, responded dramatically to prednisolone and has been maintained on a very low dose.

Since our report on fifteen cases of benign mucous membrane pemphigus, two further cases have come to our attention through the courtesy of Drs. J. Weitz and L. Berg of Worcester, Massachusetts, and Dr. C. Stoner of New London, Connecticut. The case histories were essentially similar to those reported by us. Biopsy of the first case revealed the subepithelial split seen in several of our cases. Dr. Weitz reported a dramatic response to cortisone therapy with disappearance of all oral lesions.

REFERENCES

1. Church, R. E., and Sneddon, L. B.: Ocular Pemphigus With Generalised Bullous Eruption, Brit. J. Dermat. **68**: 128-131, 1956.
2. Cross, W. G.: Oral and Buccal Pemphigus, or Pemphigoid, Proc. Roy. Soc. Med. **48**: 984, 1955.
3. Director, W.: Pemphigus Vegetans: Clinicopathologic Correlation, A. M. A. Arch. Dermat. & Syph. **66**: 343-352, 1952.
4. Klauder, J. V.: Argyria: Lupus Erythematosus of Scalp: Essential Shrivelling of Conjunctiva (Ocular Pemphigus) With Ocular, Oral and Vulvar Lesions, Arch. Dermat. & Syph. **37**: 687, 1938.
5. Klauder, J. V., and Cowan, A.: Ocular Pemphigus and Its Relation to Pemphigus of Skin and Mucous Membranes, Am. J. Ophth. **25**: 643-662, 1942.
6. Lever, W. F.: Oral Lesion in Pemphigus, Am. J. Orthodontics & Oral Surg. **28**: 569-580, 1942.
7. Lever, W. F.: Pemphigus, Medicine **32**: 1-123, 1953.
8. Lever, W. F.: Pemphigus: Histopathologic Study, A. M. A. Arch. Dermat. & Syph. **64**: 727-753, 1951.
9. Lever, W. F.: Pemphigus Conjunctivae With Scarring of Skin: Report of 3 Additional Cases, Arch. Dermat. & Syph. **49**: 113-117, 1944.
10. Lever, W. F., and Talbott, J. H.: Pemphigus: Historical Study, Arch. Dermat. & Syph. **46**: 800-823, 1942.
11. Lever, W. F., and Talbott, J. H.: Pemphigus: Clinical Analysis and Follow-Up Study of 62 Patients, Arch. Dermat. & Syph. **46**: 348-357, 1942.
12. McCarthy, P. L., and Shklar, G.: Benign Mucous-Membrane Pemphigus, New England J. Med. **258**: 726-731, 1958.
13. Morris, M., and Roberts, H. L.: Pemphigus of Skin and Mucous Membrane of Mouth Associated With "Essential Shrinking" and Pemphigus of Conjunctiva, Brit. J. Dermat. **1**: 175-181, 1888-89.
14. Nettleship, E.: Case of Pemphigus Affecting Skin and Conjunctiva and Some Other Mucous Membranes, Tr. Ophth. Soc. U. Kingdom **24**: 22-24, 1903-1904.
15. Senear, F. E.: Chronic Pemphigus Vulgaris, A. M. A. Arch. Dermat. & Syph. **65**: 429-439, 1952.
16. Thost, A.: Über Chronischen Pemphigus der Schleimhaute, Monatschr. Ohrenh. **30**: 165-174, 224-231, 1896.
17. Thost, A.: Der Chronische Schleimhautpemphigus der Oberen Luftwege, Arch. Laryng. u. Rhin. **25**: 459-478, 1911.
18. Thost, A.: Über Schleimhautpemphigus, Arch. Laryng. u. Rhin. **31**: 599-631, 1917-18.
19. Wichmanns, J. E.: Beitrag zur Kenntniss des Pemphigus, Erfurt, 1791, G. A. Keyser.
20. Wichmanns, J. E.: Ideen zur Diagnostik: Beobachtenden Aerzten Mitgetheilet. Vol. I. Hannover, Germany, 1794-1802, Helwing, p. 89.

PHARMACOLOGY AND THERAPEUTICS

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CLINICAL LABORATORY STUDIES ON A NEW TOPICAL ANTIBIOTIC: THIOSTREPTON

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(With the Assistance of Ana Tiburcio)

THIOSTREPTON[1-3] is an extremely active antibiotic principle obtained from an unidentified strain of streptomyces isolated from a New Mexico desert soil sample. Its in vitro spectrum, penicillin-like, is essentially limited to the gram-positive cocci and the neisseriae. Initial tube dilution and disc sensitivity studies[4] indicate also that the spectrum is very similar to that of penicillin. Pagano, Weinstein, Stout, and Donovick,[1] who first described Thiostrepton, have also studied the characteristics of this streptomyces species and have described the solvent requirements of Thiostrepton, paper chromatography studies, agar diffusion and tube dilution assays, stability, and minimal inhibitory concentration of Thiostrepton against various microorganisms. The antibiotic was observed to be primarily bacteriostatic. It was found to be stable in simulated gastric and intestinal juices, feces, urine, and blood plasma. Further details concerning the isolation and characterization of crystalline Thiostrepton have been reported by Vandeputte and Dutcher.[3]

It is readily obvious that it would be most desirable to have for use in the treatment of accessible superficial infections of the oral cavity and pharynx an additional effective topical antibiotic which would be topically active with concomitant relative *absence* of activity following ingestion. Preliminary laboratory studies indicate that Thiostrepton may be such an agent. Because of its marked insolubility and its lack of absorption through the gut, no parenteral or systemic oral dosage form is anticipated; nor, for similar reasons, are systemic sensitization reactions expected when this antibiotic is administered for topical oropharyngeal therapy.

From the Institute of Cancer Research, College of Physicians and Surgeons, Columbia University.

Thiostrepton ointment used in this study was supplied by the Squibb Institute for Medical Research, New Brunswick, New Jersey.

This study was undertaken to investigate the effect of Thiostrepton on various organs and vital physiologic processes following topical administration to the oral mucous membranes as determined by hematologic studies, blood chemistry, and urine determinations. In this investigation the effects of both topical absorption and systemic absorption were studied concomitantly after the oral topical application of Thiostrepton and following its ingestion over a period of therapy arbitrarily fixed at one week.

Thus, this study was intended to cast some light upon the possible occurrence of undesired side reactions or other changes resulting from low-dosage oral therapy with this compound. Our findings are reported herewith.

METHODS

This study was concerned with twenty-five adults (twenty-four men and one woman). At the time of the study, all were patients in the Francis Delafield Hospital. The age, sex, and various medical and surgical diagnoses for these patients, constituting their chief causes of hospitalization are presented in Table I. Oral disturbances were not directly responsible for any of the patients being hospitalized.

TABLE I. MEDICAL AND/OR SURGICAL DIAGNOSIS CONSTITUTING CHIEF CAUSE OF PATIENT'S PRESENT HOSPITALIZATION

CASE NO.	AGE	CHIEF CAUSE OF HOSPITALIZATION
1	71	Carcinoma of right kidney; metastasis to right hip
2	56	Benign hypertrophy of prostate; chronic balanitis
3	52	Urethral strictures
4	59	Benign hypertrophy of prostate
5	62	Cancer of prostate
6	50	Benign hypertrophy of prostate
7	46	Benign hypertrophy of prostate; chronic prostatitis; urethritis
8	59	Hypertrophy of prostate; pneumonitis
9	63	Prostatitis, chronic; benign hypertrophy of prostate
10	51	Chronic prostatitis
11	56	Chronic cystitis; hypertrophy of bladder wall
12	64	Carcinoma of prostate with metastasis to skin and rectum
13	55	Left epididymal and testicular abscess
14	63	Benign hypertrophy of prostate; inguinal hernia
15	69	Benign hypertrophy of prostate
16	53	Prostatectomy; orchiectomy, bilateral
17	49	Benign hypertrophy of prostate
18	62	Benign hypertrophy of prostate
19	72	Benign hypertrophy of prostate; chronic prostatitis
20	73	Carcinoma of prostate; urethral stricture; nonfunctional right kidney
21	53	Hypernephroma of right kidney; metastasis to right lung
22	51	Benign hypertrophy of prostate
23	52	Benign hypertrophy of prostate
24	63	Tuberculosis of the lungs; calculus in kidney; suspected carcinoma of urinary bladder
25	59	Urethral stricture; chronic bronchitis

Prior to therapy patients were studied by means of a battery of blood and urine examinations (in the fasting state) including in each instance nearly all the following test procedures: blood sugar, nonprotein nitrogen,

TABLE IV. DETAILED CLINICAL LABORATORY DATA OBTAINED BEFORE AND AFTER THE ORAL ADMINISTRATION OF 100 MG. OF THIOSTREPTON IN DIVIDED DOSAGE OVER A PERIOD OF ONE WEEK TO TWENTY-FIVE PATIENTS

PATIENT NO.		FBS (MG. %)	NPN-BUN (MG. %)*	PROTHROMBIN TIME (SECONDS) PRO-THROM BIN	PROTHROMBIN TIME (SECONDS) CON-TROL	TOTAL PRO-TEIN (%)	CEPH-ALIN FLOC-CULA-TION	ALKALINE PHOSPHA-TASE (UNITS)†	BILIRUBIN (MG. PER 100 C.C. SERUM) DIRECT	BILIRUBIN (MG. PER 100 C.C. SERUM) TOTAL	BILE	UROBILINO-GEN DIL.
1	Before	113	N20	15.9	14.4	6.1	+	B3.0				
	After	115	B16.1	15.8	14.0	6.8	+–	K8.5		0.1	Neg.	Pos. 1:60
2	Before	100	N25	Clotted		7.0	–	B1.9				
	After	120	B15.8	14.0	14.0	7.2	–	K7		0.103	Neg.	Pos. 1:80
3	Before	94	N15.2	18.0	14.4	6.8	+–	B1.7				
	After	120	B19	14.8	14.0	7.5	–	K3.0	0	Trace	Neg.	Neg.
4	Before	103	N12.6	17.2	14.4	7.9	–	B3.3				
	After	125	B23	14.0	14.0	7.4	–	K10.5		0.103	Neg.	Pos. 1:20
5	Before	92	N29			6.6	–	B2.2				
	After	135	B20.2	16.5	14.0	5.8	–	K4		0.3	Neg.	Pos. 1:20
6	Before	92	N23	17.6	14.4	7.6	–	B3.1		0.3		
	After	110	B25.4	19.0	14.0	6.4	–	K12.0		0.6	Neg.	Neg.
7	Before	87	N17	14.4	14.8	6.8	1+	B3.1				
	After	105	B16.3	13.0	13.0	6.4	–	K2.0	0	Trace	Neg.	Pos. 1:80
8	Before	86	N20	15.1	14.5		1+	B4.7		0.3		
	After	110	B17	14.1	13.0	6.6	2+	K2.0	0	Trace	Neg.	Pos. 1:40
9	Before	135	N24	15.6	14.6	7.7	–	B Normal				
	After	105	B9.9	13.5	13.0	10.5	–	K5.6	0.4	0.8	Neg.	Neg.
10	Before	83	N29	17.2	15.0	7.4	2+	B Normal				
	After	95	B19	15.5	13.0	6.1	2+	K3.0	0.2	0.3	Neg.	Pos. 1:40
11	Before	94	N21			7.6	3– 4+	B –				
	After	100	B17	15.0	13.0	6.6	2+	K3.0	0	0.3	Neg.	Pos. 1:20
12	Before	91	N17	15.5	15.0	6.5	+	B10.8				
	After	110	B12.6	13.5	13.0	5.9	–	K3.5	0	Trace	Neg.	Pos. 1:60
13	Before	97	N22	15.0	14.6	7.3	–	B Normal				
	After	95	B11.3	14.8	13.0	6.5	–	K10.5	0	0.3	Neg.	Pos. 1:40
14	Before	88	N26	Clotted		6.9	–	B Normal				
	After	110	B12	15.0	13.0	6.2	3+	K6.0	0	Trace	Neg.	Neg.
15	Before	89	N24	14.2	14.2	6.8	–	B Normal				
	After	105	B12.6	14.7	13.0	6.2	–	K5.0	0.5	0.9	Neg.	Pos. 1:60
16	Before	98	N24	15.0	14.0	7.1	–	B Normal				
	After	100	B17.5	14.0	13.0	6.4	–	K7.0	0	Trace	Neg.	Neg.
17	Before	81	N29	15.6	14.8	8.3	2+	B Normal				
	After	100	B10.5	16.5	15.0	7.4	3+	K7.5	0	0.2	Neg.	Pos. 1:128
18	Before	92	N17	15.0	15.0	8.0	–	B Normal				
	After	95	B19.0	15.0	15.0	7.2	–	K5.0	0	0.2	Neg.	Pos. 1:160
19	Before	95	N24	Clotted		7.2	–	B Normal				
	After	100	B19.7	14.0	15.0	5.9	2+	K3.0	0.2	0.5	Neg.	Pos. 1:1,280
20	Before		N20			5.5	+– 1+	B Normal				
	After	85	B18.3	15.0	15.0	4.9	–	K9.0	0	Trace	Neg.	Pos. 1:20
21	Before	85	N23	16.9	15.0	7.2	+	B Normal				
	After	90	B14.3	16.0	15.0	6.8	–	K12.0	0.1	0.2	Neg.	Pos. 1:640
22	Before	95	N27	Overdil.		6.3	–	B Normal				
	After	90	B12	15.5	15.5	5.8	3+	K5.0	0	Trace	Neg.	Neg.
23	Before	104	N27	Overdil.		7.1	–	B Normal				
	After	100	B15.2	15.5	15.5	6.9	–	K7.0	0	Trace	Neg.	Neg.
24	Before	100	N31	14.3	15.0	7.8	–	B Normal				
	After	110	B20.2	15.6	15.6	6.7	–	K8.5	0.1	0.2	Neg.	Neg.
25	Before	71	N25	15.2	14.8	6.9	–	B Normal				
	After	75	B15.8	15.5	15.5	6.2	+–	K5.0	0	Trace	Neg.	Pos.

*NPN-BUN column: N = NPN; B = BUN.
†Alkaline phosphatase column: B = Bodansky units; K = King-Armstrong units.

TABLE III. DETAILED CLINICAL LABORATORY DATA OBTAINED BEFORE AND AFTER THE PERIOD TO

PATIENT NO.		COMPLETE BLOOD COUNT								SPECIFIC GRAVITY	REACTION	ALBUMIN
		HB.	W.B.C.	R.B.C.	N.	E.	L.	B.	M.			
1	Before	7.0	6,550		57(2-55)	2	36	2	3	1.020	Acid	-
	After	13.2	7,650		61(5-56)	1	31		1	1.017	Acid	+
2	Before	12.8	7,200	4.24	53(11-42)	3	37	1	6	1.026	Acid	-
	After	12.4	7,350	4.29	60(13-47)		31	1	8	1.015	Acid	-
3	Before	11.8	5,400	3.90	53(5-48)	3	36	1	7	1.010	Alkaline	-
	After	12.4	10,700	4.25	77(7-70)	1	14		7	1.014	Acid	2+
4	Before	14.4	8,900		66(6-60)	8	22	2	2	1.012	Acid	-
	After	14.4	9,500		57(5-52)	7	31	2	3	1.010	Acid	1+
5	Before	13.0	6,050		70(18-52)	1	29			1.025	Acid	-
	After	11.2	10,650	3.78	87(11-76)		8		5	1.006	Acid	-
6	Before	11.2	4,350	3.99	61(8-53)	6	26		5	1.010	Alkaline	-
	After	11.9	11,500	4.13	73(3-70)	1	23	1	1	1.010	Acid	2+
7	Before	10.8	7,650	3.51	78(14-64)	1	20		2	1.010	Acid	-
	After	12.2	11,500	4.23	72(12-60)	4	17		7	1.018	Acid	-
8	Before	9.2	17,050	3.54	79(15-64)		20		1	1.010	Alkaline	-
	After	11.0	8,950	4.08	64(9-55)	2	29		5	1.010	Acid	-
9	Before	11.0	21,300	4.11	90(28-62)		6	1	3	QNS	Acid	1+
	After	11.4	9,200		77(17-60)	3	18		2	1.010	Acid	3+
10	Before	13.8	7,000		50(8-42)	1	41		8	1.023	Acid	-
	After	13.4	6,400		55(7-48)	4	38	1	4	1.015	Acid	-
11	Before	12.8	7,850		66(6-60)	6	21	1	6	QNS	Alkaline	-
	After	11.9	7,300	4.27	61(14-47)					1.024	Alkaline	-
12	Before	12.4	5,900	4.19	70(15-55)	2	24		4	1.010	Acid	2+
	After	10.3	8,000	3.12	82(5-77)		12		6	1.015	Acid	-
13	Before	11.9	10,700	4.39			5		2	1.015	Acid	-
	After	12.2	10,000	4.55	81(15-66)		18		1	1.018	Alkaline	-
14	Before	14.9	10,650		56(12-44)	4	36		4	1.020	Acid	-
	After	14.7	12,700		67(17-50)	1	28		4	1.006	Acid	2+
15	Before	14.7	5,400		60(14-46)	3	33		4	1.025	Alkaline	-
	After	12.2	6,200	4.37	77(11-66)	1	30		2	1.012	Alkaline	1+
16	Before	13.0	9,500		67(1-26-40)	3	24		6	1.013	Alkaline	-
	After	15.0	9,500		85(18-67)	1	12		3	1.010	Acid	-
17	Before	11.0	8,850	3.34	66(12-54)	1	28		4	1.010	Acid	-
	After	11.0	7,750	3.63	73(7-66)	1	26		6	1.017	Acid	-
18	Before	12.6	10,000		73(11-62)	1	2		5	1.012	Alkaline	1+
	After	13.0	10,350		78(8-70)	1	18		3	1.020	Acid	-
19	Before	13.8	5,000		66(17-49)	2	30		2	1.018	Alkaline	1+
	After											
	After	13.0	6,500		68(10-58)	2	25		5	1.010	Acid	-
20	Before	10.3	9,000	3.43	81(20-61)		16		3	QNS	Acid	1+
	After	8.7	16,500	2.81	90(21-69)		5		5	1.016	Acid	-
21	Before	13.4	15,150		87(31-56)		10		3	1.012	Alkaline	-
	After	13.4	10,750		76(12-64)	3	17		7	1.010	Acid	-
22	Before	14.2	6,900		72(16-56)	3	23		2	1.010	Alkaline	1+
	After	14.7	7,850		83(4-79)		17			1.016	Alkaline	-
23	Before	11.9	9,450	4.18	80(21-59)		17		3	1.017	Acid	-
	After	12.6	9,560	4.44	63(10-53)	5	27	1	4	1.016	Acid	1+
24	Before	11.4	5,050	4.27	67(8-59)	5	22		5	1.020	Acid	2+
	After	11.9	5,650		80(11-69)	1	18		1	1.016	Alkaline	3+
25	Before	12.2	4,150	3.83	54(8-46)	2	44			1.006	Alkaline	1+
	After	11.9	10,050	3.91	74(7-67)		23	3		1.012	Alkaline	2+

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ORAL ADMINISTRATION OF 100 MG. OF THIOSTREPTON IN DIVIDED DOSAGE OVER A ONE-WEEK TWENTY-FIVE PATIENTS

URINALYSIS								
GLUCOSE	BACTERIA	W.B.C. HIGH-POWER FIELD	R.B.C. HIGH-POWER FIELD	EPITHELIAL CELLS	OTHER	PLATELETS ×1,000	ESR (MM. PER HR.)	HCT PACKED CELL VOLUME (PER CENT)
–				Occasional	Triple PO_4 crystal		43	
+	Rare	1-3				198	26	44.0
–	Rare	3-4			Mucus threads		29	
–	Rare			Rare		166	26	40.0
–	Rare			Rare	Triple PO_4 crystal		19	
2+	Rare	5-7	Loaded	Occasional		194	19	42.5
–	Rare	2-5		Occasional			20	
1+		1-2	Loaded	Rare		156	31	47.5
–	Some			Rare			10	
–	Rare	2-5	3-5			167	53	34.0
–	Much			Occasional			67	
2+	Rare	10-16	75-100			252	68	35.0
–		Rare		Yes	Ca oxalate		39	
–	Loaded		10-12		Triple PO_4 crystal	180	43	41.0
–		2-3	Rare	Occasional			115	38.0
–	Rare					360	62	39.0
1+	Loaded	50-70	3-5				75	
3+	Some	3-5	Loaded			464	26	40.5
–	Rare			Rare			26	
–	Some			Occasional	Unidentified crystal	106	39	44.0
–	Much	Rare		Rare			1	Clotted
–	Loaded		10-12		Triple PO_4 crystal	208	60	38.0
2+		3-6	Loaded	Occasional			15	
–	Loaded	25-30		Moderate	Some large clumps, mucus threads	233	80	33.5
–	Much		Rare	Moderate			68	
–		0-1	Rare	Occasional	Mucus threads	236	54	44.0
–	Moderate		1-2	Occasional				
2+	Moderate	15-20	Many			226	34	46.0
–	Loaded				Triple PO_4 crystal		7	
1+	Moderate	Rare	3-6			262	22	41.0
–		Rare		Occasional				
–					Mucus threads	370	24	44.0
–	Some	8-10	Rare				45	
–		Rare		Occasional	Ca oxalate crystal	262	59	36.0
1+		0-1	Rare		Amorphous PO_4 crystal		92	
–				Occasional		230	55	45.5
1+	Much				Triple PO_4 crystal		13	
					Amorphous PO_4 crystal			
–	Some	1-2			Ca oxalate crystal	194	5	43.0
1+	Much	35-40	10-12					
–	Much	10-15	15-25	Moderate		200	76	30.0
–	Much	10-15	75-100				40	
–		1-2		Occasional	Ca oxalate crystal	238	59	44.0
+	Rare	2-4	3-5		Mucus		9	
–	Rare			Occasional		138	11	43.5
–	Rare				Amorphous urates		15	
+	Rare	1-2	10-15		Amorphous urates	510	33	43.0
+	–	Many	Loaded	Occasional			53	38.5
+	–	12-20	Loaded			188	57	39.0
+	–	20-25	10-12	Loaded			35	
+	Rare	3-5	4-8		Mucus threads	142	46	38.0

prothrombin time, total protein, cephalin flocculation, alkaline phosphatase, bilirubin, urobilinogen, complete blood count, platelet count, hematocrit, erythrocyte sedimentation rate, hemoglobin, and routine urinalysis.

Subsequent to the initial battery of tests, Thiostrepton was administered to each patient in the form of a 1.0 per cent ointment (prepared in Plastibase). It was administered on an experimental basis four times a day and applied in each instance to an area of superficial infection (usually chronic marginal gingivitis or other periodontal disease) in a total dosage of approximately 1.43 grams per day for a period of seven days. Thus, each patient ultimately was treated with a total of 10 grams of the 1.0 per cent ointment, or 100 mg. of Thiostrepton, over the one-week period. The application of the medication was supervised routinely by the nursing staff.

Immediately following the conclusion of the period of therapy (again in a fasting state), the series of blood and urine studies described above was repeated for each patient.

RESULTS

A comparative study* of the "before and after" blood and urine test values obtained in our laboratories following the one-week period of drug therapy suggests that the topical oral administration of Thiostrepton in a 1.0 per cent concentration as an ointment at a daily dosage of 1.43 grams in divided dosage four times daily did not result in any discernible noteworthy deviation from normal in these patients. All tests remained relatively within the accepted normal range. No pattern of deviation from the original findings was evident in the posttherapy findings when they were compared with the pretherapy values. Those transient individual deviations which were noted were readily accounted for by such operative or other interventions as were unavoidably superimposed because of the actual cause of the patient's hospitalization (prostatic biopsy, etc.) upon the therapy picture.

No evidence of irritation, sensitivity, inflammation, or any other deleterious effect on the oral mucous membranes was observed during or after therapy. No allergic, idiosyncratic, or other evidences of intolerance were noted.

DISCUSSION

In terms of the therapy of those oral or pharyngeal infections for which *systemic* antibiotic therapy is neither indicated nor desired, it is obvious that a local *topical* antibacterial action may nevertheless be desirable. This action should preferably be without any concomitant systemic activity (with attendant possibilities of systemic sensitization, etc.) resultant from the ingestion of that material which is inadvertently swallowed following the gradual dissolution or displacement of the antibiotic troche or ointment within the mouth.

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*All blood and urine studies reported on here were performed under the direction of Dr. George Hyman, Associate Visiting Physician, in charge of Hematology Laboratory, Francis Delafield Hospital, to whom we are also indebted for the interpretation of and consultation concerning these data.

A low incidence of gastrointestinal and other side reactions, the possibility of the above-mentioned relative absence of systemic sensitization owing to lack of gut absorption, the minimal disruption of the essentially resistant gut flora, and a high degree of local tissue tolerance at high concentrations of antibiotic are the seemingly pertinent characteristics of this agent which may also permit effective antibacterial action at such relatively higher antibiotic formulation concentrations as may be required for the effective treatment of superficial pharyngeal, oral, and dermal infections. The absence of a disagreeable taste should furthermore permit the use of this antibiotic in various oral dosage forms without the inclusion of those excipients which may have contributed to the side reactions often seen with other topical (oral) antibiotic preparations. Since Thiostrepton is expected to be limited by its physical properties to topical application, its use in this manner would not be contraindicated because of the possibility of the production of microorganisms resistant to an antibiotic (Thiostrepton) which could be administered systemically later if needed.

Laboratory evidence in animals also seems definitely to point to the inactivity systemically (upon ingestion) of Thiostrepton, representing probably either inactivation in the gut or a failure of absorption through the intestinal mucous membranes. The lack of effect on the bodily physiology reported in this article may thus possibly also reflect essentially no more than such a lack of absorption.

Continuing studies concerned with the therapeutic effectiveness of this compound will be reported upon in a separate communication.

SUMMARY

Thiostrepton, a new antibiotic, has been suggested as being highly active topically but inactive in terms of systemic therapy when administered orally and ingested. Detailed blood chemistry, hematology, and urine studies were undertaken in twenty-five patients in order that any undesirable systemic effects on physiologic processes following the topical oral administration of Thiostrepton in human beings might be observed.

Our findings indicate that no alteration in general body function and no untoward reactions occurred as the result of the topical oral administration of approximately 1.43 grams per day of a 1 per cent Thiostrepton ointment in divided doses for a period of one week.

The authors express their appreciation to Drs. John Groel and Joseph Pagano for their assistance in these studies. Grateful acknowledgment is also made to Miss Evelyn Wirth, Mrs. Eileen Geller, and Mrs. Helene W. Kutscher for their assistance.

REFERENCES

1. Pagano, J. F., Weinstein, M. J., Stout, H. A., and Donovick, R.: Thiostrepton, a New Antibiotic. I. In Vitro Studies. In Welch, H., and Martí-Ibañez, F. (editors): Antibiotics Annual 1955-1956, New York, 1956, Medical Encyclopedia, Inc., p. 554.
2. Steinberg, B. A., Jambor, W. P., and Suydam, L. O.: Thiostrepton: a New Antibiotic. III. In Vivo Studies. In Welch, H., and Martí-Ibañez, F. (editors): Antibiotics Annual, 1955-1956, New York, 1956, Medical Encyclopedia, Inc., p. 562.

3. Vandeputte, J., and Dutcher, J. D.: Thiostrepton, a New Antibiotic. II. Isolation and Chemical Characterization. In Welch, H., and Martí-Ibañez, F. (editors): Antibiotics Annual, 1955-1956, New York, 1956, Medical Encyclopedia, Inc., p. 560.
4. Kutscher, A. H., Seguin, L., Rankow, R., and Piro, J. D.: Thiostrepton, a New Antibiotic; Disc Sensitivity Studies, Antibiotics & Chemother. **8**: 576, 1958.

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A DEVICE FOR CENTERING AND ANGULATING X-RAYS IN ORAL ROENTGENOLOGY

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DENTAL roentgenology has attracted considerable attention during the past several years because of possible radiation hazards and through attempts to improve roentgenographic film quality. The dangers of x-rays have been emphasized by both accurate and erroneous reporting over radio and television and in the lay press; a "radiation consciousness" has been created in the lay public. Fortunately, the profession has long been aware of the dangers and has taken steps to reduce them. Improvement in the quality of roentgenograms has also been a goal of long standing, and many of the techniques and armamentaria that have been developed to reduce radiation hazards are mutually advantageous in improving film quality. Progress has been made in obtaining the profession's acceptance of increased target-to-film distance procedures; this, combined with the use of faster films, has been a forward step toward superior roentgenograms and a minimization of tissue insult.

Up to the present, most dental x-ray apparatus has been manufactured on the assumption that it will be used with an 8 inch target-to-film distance. Consequently, machines have been designed with a pointed cone on the tube head for use at this 8 inch distance. Now, with the trend toward increased use of the long cone or paralleling technique in which the target-to-film distance is increased to 16 or 20 inches, various difficulties arise.

The first problem is that of aiming the tube head properly so that the central ray passes through the center of the film; this has been complicated by the use of lead diaphragms introduced in the tube head to reduce the diameter of the x-ray beam and thus avoid unnecessary exposure to the patient's skin and underlying tissues. However, reduction of radiation coverage to an area just slightly greater than the surface of the film makes it imperative that the beam be aimed accurately; otherwise, parts of the film will be unexposed.

Another problem associated with increased target-to-film distance is that of angulating the tube in the correct horizontal position in order to prevent undesirable overlapping of teeth. When done without a guide, this is often a hit-or-miss setting. The determination of exact target-to-film distances for purposes of standardization and duplication is also essential.

Fig. 1.—Device attached to tube head.

Fig. 2.—Aiming central ray.

One solution to these problems has been the substitution of a special long cone for the standard pointed cone. This solves all of the above-mentioned difficulties as long as it is desirable and feasible to use the machine at a constant

target-to-film distance; however, its inflexibility is a serious drawback. Some techniques are better carried out at a shorter target-to-film distance than others. In many offices the physical setup is such that it is impractical to use a 20 inch target-to-film distance. The maximum possible distance may be 17, 15, or even 12 inches unless a cumbersome rearrangement of the chair and the patient is made. For some special procedures, the operator may want to use a target-to-film distance even greater than 20 inches.

The need for a device that will enable one to aim the tube head properly over a large range of target-to-film distances is obvious. Such a device is available* and can be easily attached to any tube head. The device consists of an adjustable collar (Fig. 1) which can be fitted to the tube heads of various manufacturers. Attached to this collar is a yoke carrying a telescoping pointer.

Fig. 3.—Pointer lifted up before exposure.

A finger-stop holds the yoke so that the pointer is in the direct path of the central ray. The pointer can be collapsed (Fig. 2) and extended within a range of 12 to 20 inches. Calibrations on the pointer make it possible to preset it at any desired position or to measure and record the distance being used after the tube head has been positioned. When the tube is correctly positioned, the pointer is merely collapsed and lifted up out of the way (Fig. 3). Obviously, a visible pointer representing the central x-ray beam makes for more precise horizontal and vertical angulating. The flexibility of this device makes it a valuable addition to the armamentarium of the general practitioner who is faced with a great variety of technical roentgenographic problems. (See Associate Editor's note.)

*Furnished by the Grafax Instrument Company, New York, New York.

SUMMARY

There has been much recent progress in reducing radiation hazards and in increasing the quality of roentgenograms. New techniques associated with this progress have created problems directly related to angulating the x-ray machine. A device which solves some of the problems concerned with angulation and centering of the x-ray beam has been described in this article.

REFERENCES

1. Fixott, H. C., Claycomb, C. K., and Pflugrad, A.: Dental Office Radiation Hazards, Oregon D. J. **25**: 2-4, 1956.
2. Kirsh, I. E.: Radiation Dangers in Diagnostic Radiology, J. A. M. A. **158**: 1420-1423, 1955.
3. Hielscher, W.: A New Roentgenographic Technic for Practicing Dentists, Deutsche Zahnarzteble **9**: 885, 1955.
4. Freese, A. S.: The Long Cone Technique in Temporomandibular Joint Roentgenography, New York State D. J. **24**: 248-249, 1958.
5. Budowsky, J., Kutscher, A. H., Mercadante, J., Cuttita, J., Piro, J. D., and Earnest, F. A.: Effect of Increasing Target to Film Distance on Intraoral Roentgenographs, New York State D. J. **24**: 243-246, 1958.
6. McCormack, D. W.: Mechanical Aids for Obtaining Accuracy in Dental Roentgenology, J. Am. Dent. A. **40**: 144-153, 1950.
7. Spear, L. B.: Need for Precaution in Dental Roentgenography, J. Am. Dent. A. **51**: 7-12, 1955.
8. A Practical Manual on the Medical and Dental Use of X-rays, Bulletin sponsored by the American College of Radiology and the A. D. A.

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ASSOCIATE EDITOR'S NOTE

The device described in this article is worthy of publication, but it has one major shortcoming. Changes in target-to-film distance and the size of the area to be covered at any particular target-to-film distance necessitate the use of a lead iris diaphragm or of readily interchangeable lead diaphragms having various-sized openings for proper beam columnization. Unless the device described incorporates such a mechanism, it has no particular advantage over fixed-length plastic cones equipped with suitable diaphragms. The suggestion is therefore made to the author and to the equipment manufacturer that either a slot be provided in the pointed plastic cone which would permit the interchange of appropriate lead diaphragms or a lead iris diaphragm be incorporated as an integral part of the localization device.

KILOVOLT (PEAK) AND THE SENSITIVITY OF VERY FAST DENTAL FILMS

L. R. Manson-Hing, D.M.D., Birmingham, Ala.*

IN RECENT years dentists have had available for the production of diagnostic roentgenograms two very fast films and x-ray machines with variable kilovolt (peak) selectors. When these new films and machines are used, the quality of the diagnostic roentgenogram is affected. The quality of the diagnostic roentgenogram is judged mostly by the definition of the objects under observation; this definition can be affected by both contrast and density. The over-all density of the roentgenogram is usually controlled by the amount of radiation used. While the desired density varies with different operators, this variation is relatively small. The contrast scale varies with the KVP, the higher kilovoltages giving a longer scale of contrast. While this greater gradation of "shades of gray" is desirable, there are other factors that bear investigation when a change in KVP is considered. One such factor is the sensitivity of the film to the different qualities of x-radiation produced when the KVP is changed.

Wilsey[1] showed in 1951 that the response of a widely used film† to x-radiation varied with KVP and also varied with filtration. This film was most sensitive at 90 KVP when the x-ray beam was lightly filtered (1.5 mm. aluminum total) and at 45 KVP when the x-ray beam was heavily filtered (0.5 mm. aluminum to 0.4 mm. copper total). He also stated that other films, including the dental films, showed a similar trend. The use of fast films is the most important single factor in the reduction of the patient's dose of x-radiation during the production of dental roentgenograms. It is thus obvious that the characteristics of these films should be thoroughly investigated.

EXPERIMENTAL DATA

In this study two very fast commercial dental x-ray films‡ that have been available for the last few years have been investigated. This was done by exposing them to varying amounts of radiation at kilovoltages of 40 to 90 KVP. A General Electric Model CDX 90 x-ray machine was used and operated at 15

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*Member of the American Academy of Oral Roentgenology.
†Kodak Blue Brand.
‡Kodak Ultra-Speed; Du Pont Lightning Fast.

Ma., since the machine had the greatest calibrated KVP scale (40 to 90) at this Ma. setting. The dose delivered to the film was changed by the use of the electronic timer; the tube-film distance was kept constant at 25 inches. The total filtration of the x-ray beam was 2 mm. of aluminum (equivalent). An aperture ¾ inch in diameter was used in the lead diaphragm; most of the pointed plastic cone was cut off, thus removing all plastic from the path of the primary radiation. The film, with an ionization chamber attached, was hung in an open window. This procedure was used to cut down on scatter radiation from the walls of the room.

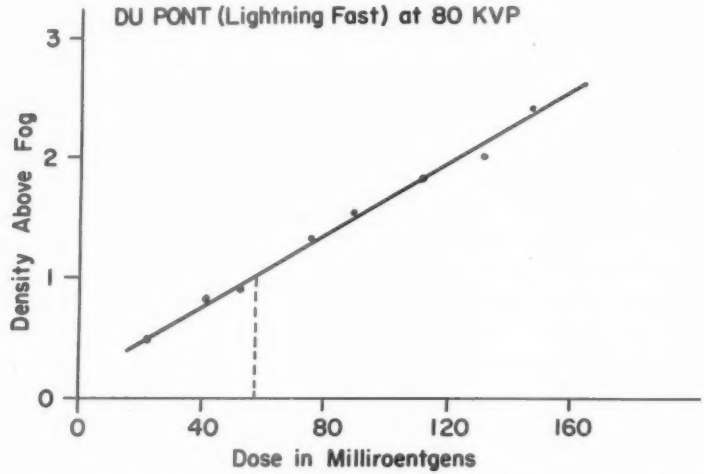

Fig. 1.—Graph showing the effect of varying amounts of 80 KVP x-rays upon the density of Du Pont Lightning Fast film.

Dose measurements were made with a 200 mr Victoreen Minometer ionization chamber, the type normally used for monitoring the personnel of diagnostic x-ray departments. The chamber was placed in the same plane as the x-ray tube (horizontally in this instance) to reduce the effect of variations in radiation intensity within the x-ray beam due to the "heel effect." The same chamber was used for all measurements; it was charged immediately before and read immediately after each exposure. The films of each make used were all of the same emulsion number, thus eliminating any variation in emulsion sensitivity due to manufacturing.

A widely used developer and fixer* were used to develop the films; the developing time for all films was five minutes at a temperature of 68° F. Agitation of the films was made uniform by hanging the film racks on a metal frame that could move all the films simultaneously. All the films of the same type were opened in total darkness and processed together at the same time.

*Kodak liquid x-ray developer and Kodak liquid x-ray fixer.

Some unexposed films were developed along with the exposed films to determine the amount of fog on the films. The possibility of electron and x-ray backscatter from the metal foil in the dental film packets was investigated by comparing the densities obtained when films were exposed with and without the metal foil. No variation in density was observed between these films.

The density* of each film was measured on a Weston Model 877 Type 5 densitometer, and a graph plotting dose against density above fog was made for each kilovoltage used. Fig. 1 demonstrates a typical dose-density plotting. From these graphs, the dose required to produce density 1 above fog

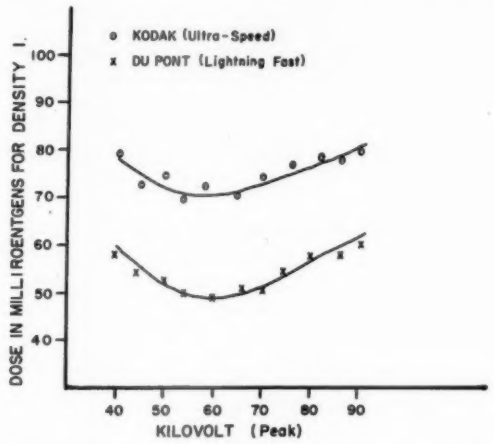

Fig. 2.—Graph showing the sensitivity of two dental films to changes in kilovoltage (peak). Density of film base plus fog = Kodak 0.2, Du Pont 0.4.

was obtained and plotted against KVP as shown in the graph in Fig. 2. Density 1 was chosen since this is the approximate over-all density of an oral roentgenogram. It can readily be seen from Fig. 2 that both of the films under investigation show a response that varies with the radiations produced at different KVP settings of the dental machine. These films were most sensitive to 60 KVP radiations and least sensitive at 40 and 90 KVP. The variation was approximately 20 per cent of the dose required to give a density of 1.

It is obvious that if these films are to be used for dosimetric measurements in dental offices, they must be calibrated to the quality of the radiation that they are going to receive. If this is not done, there might be an error of as much as 20 per cent from this factor alone, even when calibrated to the x-ray beam of a dental machine. Another field affected by this variation in response is that of diagnostic roentgenography. Since the roentgenologist is interested in the x-rays either reaching the film unchanged or being completely absorbed

*Photographic density controls the amount of light that passes through a film. The densitometer is of the photoelectric, direct reading type, calibrated in terms of diffuse transmission density.

by the object under observation, there would appear to be an optimum KVP setting of 60 on the dental machine whenever these films are used for this purpose.

CONCLUSION

1. The response of the two very fast dental films varies with different qualities of x-radiation that can be encountered in a dental office.

2. There exists the possibility of a 20 per cent error due to differences in radiation quality whenever these films are used for dosimetric measurements of dental x-ray installations.

3. When these films are used in diagnostic roentgenography the factor of film response would indicate an optimum KVP of about 60 on dental machines.

REFERENCE

Wilsey, R. B.: The Use of Photographic Films for Monitoring Stray X-rays and Gamma Rays, Radiology **56**: 229-241, 1951.

ORAL PATHOLOGY

LEONTIASIS OSSEA

Report of a Case

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LEONTIASISI OSSEA is a very rare condition, and the case described in this article would appear to be the first one reported from Ireland. It is of interest because the diagnosis was made chiefly from dental findings, the other details being filled in as the investigation progressed.

CASE REPORT

W. H. L., a 16-year-old boy, was referred to me for consultation on June 4, 1956, with a history of missing teeth.

History.—The patient was the youngest of three boys. At the time of his birth, which was normal and full-term, the only abnormalities evident were syndactylia of the little and ring fingers of each hand and a squint.

He had difficulty with vision from an early age and wore spectacles, but he made adequate progress in school in spite of this. He became totally blind in 1953.

The other members of the family were normal and healthy.

General Examination.—Examination revealed a fair-haired young man of medium height with a rather square set to the head, a narrow and pinched nose, and prominent lips. The forehead bulged slightly and symmetrically in both the frontal and supraorbital regions, and the angles of the mandible were extremely prominent (Fig. 1).

Shoulder movements were normal, and both clavicles were present. The syndactylia described above had been operated on (Fig. 2).

Intelligence.—The patient appeared to be of normal intelligence; he was quiet spoken with good enunciation. He had a good sense of humor, read Braille well, and demonstrated an uncanny instinct for finding his way about. He was anxious to improve his appearance and cooperated fully and willingly.

Oral Examination.—When the mouth was gently stretched, bilateral transverse facial clefts (macrostomia) were evident (Fig. 3).

The mouth was generally clean, and the tongue was normal. The oral mucosa was normal in color and distribution, and the periodontal condition was satisfactory except for

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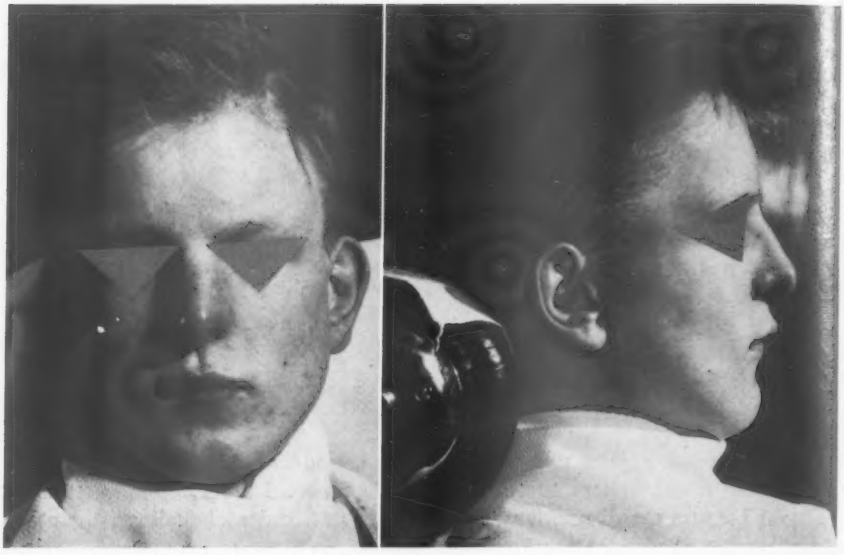

Fig. 1.—Front and side views of 16-year-old patient.

Fig. 2.—Syndactylia.

a small amount of supragingival calculus in the lower incisor region. The following teeth were present:

7 5 4 3	7
5 4 3 2 1	1 2 3 4 7

Each tooth showed marked enamel hypoplasia and brown discoloration; arrested caries in the upper molars was causing no discomfort.

Fig. 3.—Macrostomia.

Fig. 4.—Intraoral photograph showing bulges in palate representing unerupted teeth.

Occlusion: This was naturally very poor, and the elongation of the anterior alveolus had produced a very deep overbite (6 mm.).

Alveolus: The most striking changes were in the alveolar bone, which was greatly enlarged. In the molar region of the mandible, for example, the crest was 0.5 inch (1.25 cm.) in width (buccolingual), and if the buccal extension of the bone was added the measurement was 0.75 inch (1.9 cm.), while the vertical height was also greater than average.

The mandible flared outward at its angles, making them very prominent. Bulges representing unerupted teeth could be seen and palpated in the palate, which was high, and the tuberosities were enlarged (Fig. 4).

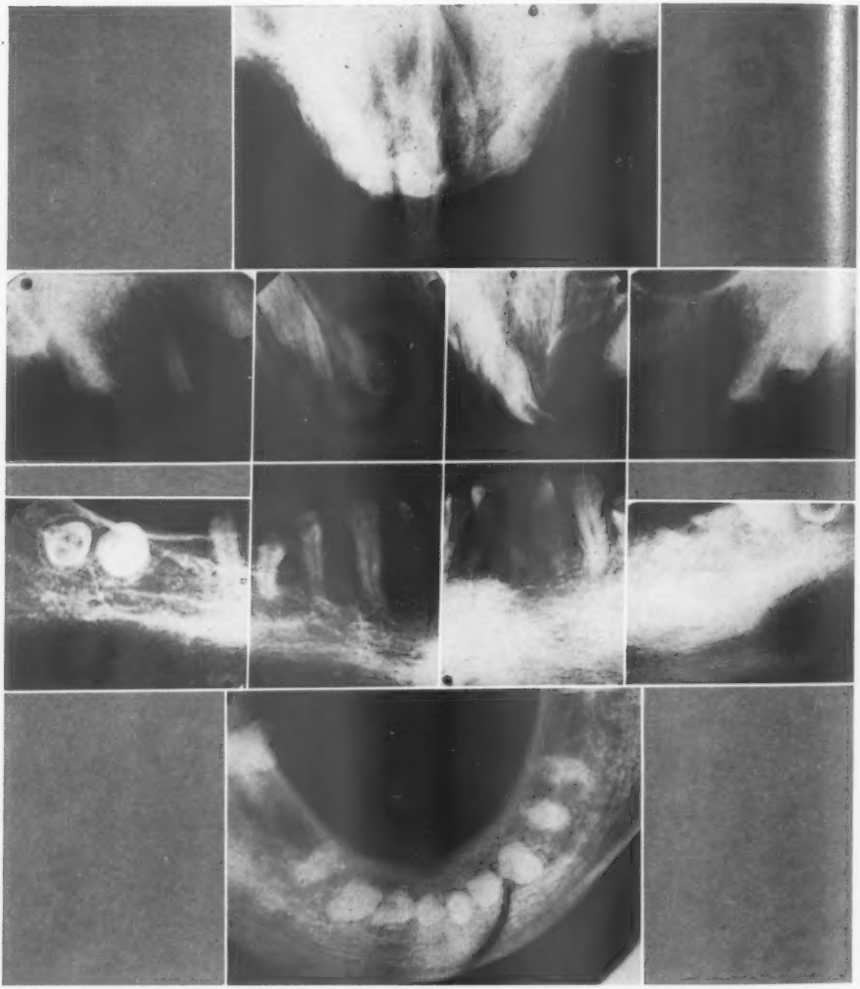

Fig. 5.—Roentgenograms of teeth.

Roentgenographic Findings.—

Intraoral films were taken, and the unerupted teeth were identified as follows:

$$\frac{8 \quad 21}{87} \Big| \frac{3 \quad 8}{\quad 8}$$

The unerupted right maxillary central incisor was a supernumerary tooth.

The teeth were normal in size, with no evidence of hypercementosis, rather pointed short roots being the rule (Fig. 5).

The alveolar bone showed a typical ground-glass shadow which, associated with the patient's age and the other findings, was suggestive of leontiasis ossea. Full plates of the skull were therefore obtained, and the report was as follows:

> There is a general increase in the thickness of the skull and facial bones, with marked reduction in the size of the frontal sinuses, sphenoids and antra, but with, as yet, only slight alteration in the orbits. The lower jaw also shows a good deal of enlargement. These findings are typical of leontiasis ossea.

These films, especially the lateral view, revealed that the thickening of the calvarium was smooth and well defined, with no sign of the irregular deposition and absorption associated with Paget's disease.

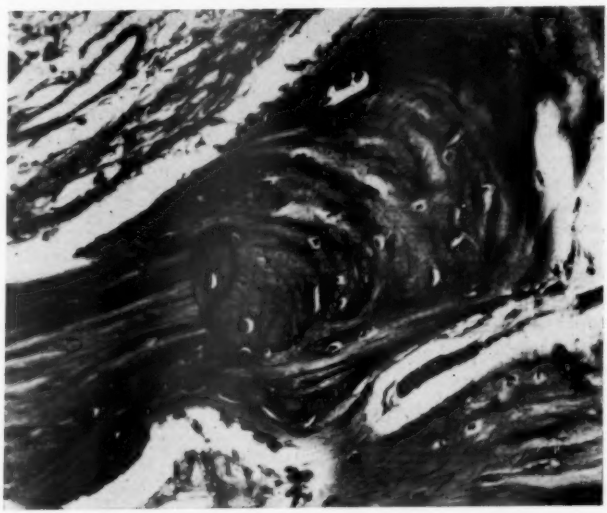

Fig. 6.—Biopsy specimen from maxilla.

Skeletal films were also taken to check the spine, long bones, hands, and pelvis, but no abnormality of any sort was detailed in either the substance or the shape of these bones.

Blood Chemistry.—The findings were as follows: serum calcium, 10.9 mg. per cent; serum phosphorus, 3.8 mg. per cent; alkaline phosphatase, 12 units (Bodansky) (normal adult range, 1.5 to 4.5 units).

Biopsy.—Following induction of endotracheal anesthesia, a portion of the upper alveolus corresponding to the size of a tooth was removed in the right premolar region. A mucoperiosteal flap was reflected, the bone was cut with chisels and burs, the edges were smoothed with files, and the flap was carefully sutured with full antibiotic cover. Bleeding and clotting were normal, and the bone cut easily like hard, thick cardboard. Healing was uneventful.

Pathologic Report (Prof. R. O'Meara): "Typical Paget type deposition with characteristic mosaic and cement lines" (Fig. 6).

Further Investigation.—The position at this stage was explained to the patient's brother, who then volunteered the information that he had the notes of the brain surgeon* who had operated on the patient in 1951. Briefly, these notes revealed that the patient was seen on Oct. 17, 1950, at the age of 11 years, with a history of blindness in the left eye for about two years. His head appeared to be rather small, and the circumference measured 20.75 inches (52.6 cm.). An ophthalmologist's report noted marked cupping of both discs, and the diagnosis of a progressive atrophic condition of the optic nerve was made. Serum calcium and phosphorus were normal, and an encephalogram showed normal ventricles. An operation was performed for decompression of the optic nerve. The significant finding, in the light of the present examination, was a thin optic nerve and narrowed optic foramina, to which reference will be made again later.

The discovery of the earlier skull measurement naturally prompted a comparison, and the circumference in December, 1957, was 22.37 inches (56.8 cm.).

Treatment.—It was evident from the start that nothing could be done for the underlying condition. The aim of treatment, therefore, was to make the patient as comfortable as possible, to improve esthetics since he wished it, and to interfere as little as possible with the bone tissue.

To this end, it was decided to remove the upper teeth under local anesthesia, one or two at a time, and to leave the unerupted teeth where they were unless they gave rise to trouble or began to erupt. There is a well-established danger of necrosis if surgical interference is made where grossly thickened bone exists, even though healing at biopsy was normal in this case.

The first extraction procedure, in which the right maxillary second molar was removed, was extremely painful in spite of a normal dose (1 ml.) of 2 per cent Xylocaine, and on the subsequent occasions larger doses were used. In spite of a waiting period of fully six minutes, anesthesia was poorer than I[1] have ever seen with this anesthetic; this was undoubtedly due to the vast increase in thickness of the bone, which prevented infiltration.

The full upper denture was fitted and cut clear of the tuberosities to prevent impingement of the lower alveolus. Reduction of the tuberosity was not justifiable at this time, for the reasons given previously. If subsequently the alveolus enlarges to such an extent that it causes discomfort or distress, an alveolectomy will be performed.

In February, 1958, a physical examination revealed no essential changes. The denture was fitting comfortably, and there was no evidence of further alveolar enlargement. The alkaline phosphatase reading was now 14.0 Bodansky units, and the acid phosphatase was 1.0 unit.

A further examination in August, 1958, revealed no physical change. At that time the skull measurement was 57.2 cm., an increase of 0.4 cm. in six months.

New skull radiographs were also taken (Figs. 7 and 8), and these showed no change in the bone structure since the original films.

DISCUSSION

Leontiasis ossea is a term invented by Virchow[2] in 1865 to describe a diffuse thickening of the skull and facial bones which gives a leonine appearance. Although this appearance had been known long before in cases of leprosy, his was the first description of a bony cause. Much confusion exists in the literature because the condition is regarded by some as a distinct entity, while more recently others have leaned toward the view that it is a clinical finding which may be brought about by a number of different causes.

Thoma[3] described a well-defined entity and reserves the term leontiasis ossea for diffuse hyperostoses of the cranium and facial skeleton caused by

*The late Mr. C. A. Calvert, F.R.C.S., of the Royal Victoria Hospital, Belfast, Ireland.

Fig. 7.

Fig. 8.

Figs. 7 and 8.—Posteroanterior and lateral views of skull.

extensive periosteal proliferation and sclerosis of the bone, specifically excluding the tumorlike hyperostoses, such as Paget's disease, which may affect any part of the skull.

He has made a detailed analysis of his own cases and those reported by others and describes certain features which he regards as typical of leontiasis ossea. In addition to the production of the leonine appearance, he explains that the sinuses may be obliterated, the orbit encroached upon, and the optic foramina contracted causing eventual blindness. He also includes in his findings expansion of the alveolus to almost double the normal size with widening and deepening of the mandible and retarded dentition (possibly because of the dense bone which hinders eruption), but he notes that the teeth do not participate in the hyperplasia and are normal in size.

Roentgenographically, the thickened, dense bone is distinguished from Paget's disease where the "cotton wool" appearance is characteristic. The calvarium may be 3 to 5 cm. thick with density in the jaws so increased as to obliterate the teeth.

Thoma recounts the history of a case which he had observed since the patient was 9 years old. In that case an enormous thickened alveolus and a high palate were supplemented later by the typical leonine appearance and marked longitudinal develoment of the head.

Very few biopsies, Thoma states, have been performed in leontiasis cases. Among those few, however, Bordenhauer and Lossen described a bone proliferation of well-calcified, irregular trabeculae lined with osteoblasts. Thoma's own biopsy findings are of considerable interest in relation to the present case. At excision, he found the bone unusually hard and not at all of the cheesy consistency seen in Paget's disease. Microscopically, he found (1) excessive formation of subperiosteal bone arranged in layers with marked osteoblastic activity and (2) thickening of the trabeculae, decreasing the size of the spaces between them. There is no evidence of absorption, and dense sclerosed bone results. The bone itself appears normal, well-calcified, and not of the woven variety; nor are there curvilinear markings to indicate rebuilding of bone, as in Paget's disease.

Stones[4] concurs in this description of bone deposition and normal type of teeth.

Cahn,[5] in a review of the jaws in generalized skeletal disease, observes that leontiasis ossea should be regarded as a localized form of Paget's disease but points out that there are now grounds for believing that it may be a variant of fibrous dysplasia of bone. Among the reasons for the latter belief is the fact that Paget's disease usually starts after the fourth decade whereas leontiasis is found in young persons.

Cahn gives an account[6] of two typical findings which may be made microscopically—(1) the typical Paget mosiac and (2) the fibrous replacement of the marrow with small islands of bone (thought to be metaplastic in origin, from connective tissue) lying in the midst of whorls of fibrous tissue

as seen in dysplasia. In one case discussed biopsies from different areas provided both of these pictures, and Cahn finds that bone at biopsy is usually soft.

Regarding alkaline phosphatase levels in the serum, Cahn states that levels are greatly elevated in Paget's disease if a number of bones are actively involved in the osteoblastic reaction, but where the disease is limited to a segment of the jaw the reaction may not be sufficient to affect the phosphatase level.

Cahn refers to the roentgenographic findings in Paget's disease, especially the "ground-glass" appearance in the maxilla where trabeculae can still be discerned, the "cotton wool" in the vault, and the widespread hypercementosis frequently seen.

Robinson and Fogel [7] report a case of the fibrous dysplasia type in a 60-year-old woman to call attention to the fact that under the heading of leontiasis ossea are grouped cases of Paget's disease and polyostotic fibrous dysplasia. Their case had "ground-glass" alveolar bone in the roentgenogram, but it does not appear to show hypercementosis except possibly to a very small degree in the area of 765. Here, too, at biopsy bone cut easily with hand pressure on a chisel. Blood chemistry was normal, and microscopically the section showed typical findings of fibrous dysplasia.

Writing recently on fibrous dyplasia and fibro-osseous lesions of neoplastic origin, both of which can cause considerable distortion of the facial skeleton, and the "ground-glass" roentgenogram, Thoma[8] makes another noteworthy observation. In fibrous dysplasia the weakness produced in developing bone is compensated by profuse cell activity with resultant distortion of contour. In tumors, on the other hand, the cells reproduce in the stage which they have originally attained and form a mass for which at first space is made by osteoclastic absorption of the surrounding bone, but later the extension of the growth produces distortion.

For the purpose of later comparison, it would be useful to consider a picture of the present concept of Paget's disease as it affects the skull and jaws.

Cooke[9] has aptly said that bone has only three reactions, no matter what their causes. It can be formed, it can be resorbed, or it can die. In fibro-osseous disease an attempt is made to reproduce the embryogenesis of membrane bone formation. True trajectories are not reached, however, and even in Paget's disease, where the most mature type of such bone is produced, it is never fully mature and functionally arranged.

In a careful survey of the findings in fifteen cases of Paget's disease with special regard to jaw involvement, Cooke[10] found the following:

Clinically, there were smooth enlargement of the alveolus leading to obliteration of the buccal undercut, rounding of the palate, and overeruption of the teeth due to increased bone formation. In all cases the inclination of the teeth eventually became palatal in the maxilla, and in the three mandibles involved the inclination became lingual in the mandible. Involvement of the mandible is not common in the experience of most writers.

Biochemically, where the skull alone was involved the serum alkaline phophatase was 20 to 30 King-Armstrong units.

Roentgenographically, an osteoporosis was seen at first in the region of the teeth. This proceeded later to radiolucency. In the mandible several cases showed the trabeculae bearing stress from the teeth taking up a parallel position, resulting in a fibrillar appearance, while the lamina dura was lost.

In the osteosclerotic stage new bone was laid down in dense sclerotic patches, but in the maxilla the increase in density was even and slight, giving the ground-glass x-ray appearance. Hypercementosis was seen in four of the seven patients with teeth, and Cooke regards resorption of teeth followed by hypercementosis as an invaluable diagnostic feature of Paget's disease in either jaw. He quotes Lucas,[11] who made a tentative diagnosis of Paget's disease from such a tooth and later confirmed it with a full investigation.

The sign was first mentioned by Rushton[12] who compared the resorption and excessive deposition of cementum on the apices of two molar teeth from a patient with Paget's disease with the bone changes elsewhere in the body. Thoma[3] and many others have described similar findings.

Spilka and Callahan[13] draw attention to the work of Meschan, who suggests that some 3 per cent of patients over 40 years of age may show some bone changes suggestive of this condition in dental roentgenograms. Spilka and Callahan advocate repeat jaw films where there is any suspicion of Paget-like lesions, such as ill-defined, nonencapsulated radiolucency, for example, to assist in early diagnosis.

They find that hypercementosis is usually, but not always, present in Paget's disease, and they confirm the homogeneous sclerosis which distinguishes leontiasis ossea from Paget's disease.

In the skull there is ill-defined thickening of the outer table with areas of radiolucency (osteoporosis circumscripta), while the deposition and resorption of bone produce the typical "cotton wool" effect on the film.

As for *histopathologic* findings, blood vessels are markedly dilated and congested, and the marrow is extremely vascular. There is danger of hemorrhage at extraction; yet, the dense sclerotic bone which may require treatment by alveolectomy is likely to sequestrate due to its own poor blood supply.

The bone changes consist of excessive lacunar resorption and apposition of an inferior type of bone involving both cancellous and cortical tissue.

This is a slow process, and the section will show indentation of the osteoclastic type with new bone being deposited in it. The new bone is formed in a coarse collagenous matrix of deposited connective tissue, and the curvilinear markings of the mosaic represent the border line between old and new bone which can cause considerable distortion of the facial skeleton.[3]

ANALYSIS OF FINDINGS IN PRESENT CASE

The condition is one of leontiasis ossea, but whether it is the entity described by Thoma or the outward manifestation of another disease, as suggested by Cahn and others, is the problem under discussion. It is evident that there

are features present which do not conform to any one of the bone dyscrasias, and a comparison of the present case with the findings in three conditions to which it bears resemblance will help to throw these points into relief.

For convenience, it is accepted that enlargement of the skull and alterations in facial contour with bulging of the supraorbital ridges are common to the conditions to be examined.

Leontiasis Ossea (as Defined by Thoma)

A. *Points Which Conform*

Age: First or second decade.

Teeth: Unerupted teeth, with no evidence of hypercementosis.

Alveolus: Gross enlargement, particularly in the mandible and maxillary tuberosities. High palate which may be partly due to elongated alveolar ridges.

Maxilla and mandible: Both involved, with flared prominent mandibular angles the most noticeable feature.

Nerve involvement: Bilateral optic atrophy and blindness, presumably following constriction of optic foramina.

Roentgenograms: The calvarium is smoothly thickened in a solid, well-calcified layer. Characteristic ground-glass appearance in intraoral films of alveolus and in occlusal views. No evidence of hypercementosis but a tendency to tapered roots of teeth, while unerupted teeth are also present. Sinuses are almost obliterated, and orbit shows early infiltration.

Blood chemistry: No definite findings are reported by Thoma, but since evidence of bone activity is not discounted, the raised alkaline phosphatase figure is not inconsistent.

B. *Points Which Do Not Conform*

Roentgenogram: Density of alveolus did not obliterate view of teeth, but this is not regarded as important.

Biopsy: At biopsy the bone had the consistency usually associated with Paget's disease and quite unlike the hard bone which Thoma contrasts clearly in the description of his own case. Microscopically, the present case showed the classical pagetoid mosaic, indicating irregular deposition and resorption of the bone, as distinct from the continuous deposition by osteoblastic activity with no evidence of resorption described for leontiasis. It is possible that further biopsies from other regions may yet show a variant of the pictures, but this is pure speculation.

Paget's Disease (Osteitis Deformans)

A. *Points Which Conform*

Teeth: Unerupted teeth may be associated with this condition.

Circumference of skull: An increase of 1.62 inches (4.2 cm.) in eight years.

Alveolus: Marked enlargement is common, especially in the maxilla, with protrusion of the incisor teeth onto the lower lip.

Maxilla and mandible: Enlargement of the maxilla, but much less commonly of the mandible, is well established.

Nerve involvement: Generally a late development, causing pain chiefly.

Roentgenograms: Ground-glass appearance and thickening of the calvarium.

Blood chemistry: Alkaline phosphatase may be raised to a level of 30 to 135 Bodansky units.

Biopsy: Absolutely characteristic in all respects, including consistency.

B. *Points Which Do Not Conform*

Age: Paget's disease is more common in women and is usually seen from about the fifth decade onward. If this is, in fact, a case of Paget's disease, it is

not unreasonable to infer that the changes seen in the paths of the optic nerves at operation in 1951, when the patient was 11½ years of age, were the first recognizable signs of the disease, which would make it the youngest case of Paget's disease to be reported in the literature, so far as I know.

Mandibular changes: Gross mandibular changes, such as were found in the present case, are rare in Paget's disease.

Nerve involvement: Blindness from narrowing of the foramina is atypical, although Thoma[14] mentions it as a complication.

Roentgenograms: The smooth thickening of the calvarium and involvement of the sinuses are the most striking differences from Paget's disease. The area in the frontal region of the present case which resembles osteoporosis circumscripta is the trephine mark from the operation performed in 1951. There is no evidence whatever of hypercementosis; quite the opposite, in fact, for the roots are thin and pointed.

Albers-Schönberg's Disease (Osteopetrosis)

A. *Points Which Conform*

Age: Childhood.

Teeth: Delayed eruption.

Alveolus: Alveolus may be extremely dense, but enlargement is not a feature.

Nerve involvement: Early closure of foramina and blindness are common.

Roentgenograms: Very great smooth, regular thickening of the calvarium with a highly calcified appearance. Sinus and orbital involvement are well established.

B. *Points which do not conform*

History of frequent fractures because of fragility of bone.

Involvement of whole skeleton.

Roentgenograms: Alveolar bone is so dense that it is hard to distinguish teeth. A characteristic club-shaped thickening and increased density of the clinoid processes produces a typical change in the sella turcica.

Blood chemistry: Raised calcium and phosphorus levels.

CONCLUSIONS

On balance, osteopetrosis appears to have little place in the differential diagnosis and, while most of the evidence is strongly in favor of the leontiasis ossea entity, the biopsy findings and bone consistency cannot be denied as evidence of Paget's disease.

The congenital irregularities (clefts, syndactylia, double lip, missing teeth, and perhaps noneruption) may be grouped together as being commonly found in association with most of the dyscrasias, but they are hardly to be regarded as having a specific connection with any one of them, interesting though they are.

It is by no means important that every diagnosis be neatly pigeonholed in its own compartment. On the contrary, cases such as this one with its dual affiliation may prove to be links which will someday show a common factor for the dyscrasias of bone and help to resolve the many differing explanations of their pathology.

Spilka and Callahan[13] state: "In the portfolio of diagnostic procedures, there is none more definitive than the tissue section, and any bone lesion whose etiology is not immediately apparent, regardless of appearance, demands histopathologic study."

If full significance is given to the biopsy and blood findings in the present case, then, because of the patient's age, roentgenograms, skull thickness, obliteration of sinuses, and bone consistency, I am disposed to classify it as leontiasis ossea with Paget's disease as the underlying cause, for the sake of description. It is neither possible nor desirable to label it beyond that point at this time. As long as the patient is available, follow-up examination, roentgenograms, and tests will be carried out, and possibly further information will be adduced which will allow a clear-cut distinction to be made.

SUMMARY

1. A case of leontiasis ossea which was primarily investigated as a result of oral findings is presented.

2. There are present atypical features which leave the diagnosis between the pathologic entity described as leontiasis ossea and the clinical appearance known as leontiasis ossea the latter of which may be due to a number of underlying causes.

3. In this case, Paget's disease is suggested as the underlying cause, for biopsy and blood findings compatible with Paget's disease are present. If this is so, the case is of interest as the patient is the youngest that I have been able to find reported in the literature.

4. Roentgenographic features and facial and dental findings typical of the pathologic entity known as leontiasis ossea are also present.

5. A survey of some of the relevant literature is included.

The author wishes to thank Mr. Fitzgerald who referred the case originally, Professor R. O'Meara and Professor W. Jessop of Dublin University for the pathologic and blood serum reports, respectively, Dr. C. McDonagh for the skull radiograph, and Mr. E. R. Roberts for the photographs.

REFERENCES

1. Cowan, A.: J. D. Res. **35**: 824, 1956.
2. Virchow, R.: Arch. f. Path. Anat., 1865.
3. Thoma, K. H.: Oral Pathology, London, 1944, Henry Kimpton, p. 349.
4. Stones, H. H.: Oral and Dental Diseases, London, 1948, E. & S. Livingstone, p. 74.
5. Cahn, L.: Ann. Roy. Coll. Surgeons England **8**: 125, 1951.
6. Cahn, L.: ORAL SURG., ORAL MED. & ORAL PATH. **6**: 202, 1953.
7. Robinson, M., and Fogel, L. J.: ORAL SURG., ORAL MED. & ORAL PATH. **9**: 817, 1956.
8. Thoma, K. H.: J. Oral Surg. **14**: 185, 1956.
9. Cooke, B. E. D.: Brit. Dent. J. **102**: 1, 1957.
10. Cooke, B. E. D.: Ann. Roy. Coll. Surgeons England **19**: 223, 1956.
11. Lucas, R. B.: J. Clin. Path. **8**: 195, 1955.
12. Rushton, M. A.: Guy's Hosp. Rep. **88**: 163, 1938.
13. Spilka, C. J., and Callahan, K. R.: ORAL SURG., ORAL MED. & ORAL PATH. **11**: 809, 1958.
14. Editorial: Paget's Disease, ORAL SURG., ORAL MED. & ORAL PATH. **11**: 807, 1958.

19 HARCOURT ST.

CLASSIFICATION OF DENTINE INTO PRIMARY, SECONDARY, AND TERTIARY*

Yury Kuttler, D.D.S., M.D., Mexico, D. F.

THE most important function of the dental pulp is the formation of dentine with which there exists such an intimate histologic and physiologic relationship that some authors consider them as two parts of the same pulp organ.

We are all aware of the existence of three distinct types of dentine, distinguished by their origin, motivation, time of appearance, structure, chemical composition, tonality, physiology, resistance, and finality. However, there exists real chaos concerning the denomination of each type. There is so much confusion that one does not always know which type is under discussion.

With the purpose of ending this confusion, and in order to avoid future difficulty, I propose to refer to these three types as primary, secondary, and tertiary dentine.

PRIMARY DENTINE

This dentine is formed by the thickening of the basic membrane between the internal enamel epithelium and the primary mesodermic pulp. First, the network of von Korff's fibers appear producing the first organic precollagenous (uncalcified) dentine that becomes the predentine. This is followed by the appearance of the dentinoblasts, and by a process not yet determined the calcification of the dentine starts.

The dentinoblastic column begins to separate gradually and dentinogenesis advances from the incisal or occlusal portion toward the apex of the tooth forming the primary dentine (Figs. 1 and 2, D^1), which has also been referred to as primitive, initial, regular, normal, physiologic, etc. In the dentine of

Presented before the Mexican Society of Endodontia, Aug. 2, 1957.
*From the book entitled *Endodoncia Práctica* (in preparation).

young persons the tubules are very numerous (15,000 to 70,000 per square millimeter), almost straight, and fairly wide, representing one-fourth of the dentine.

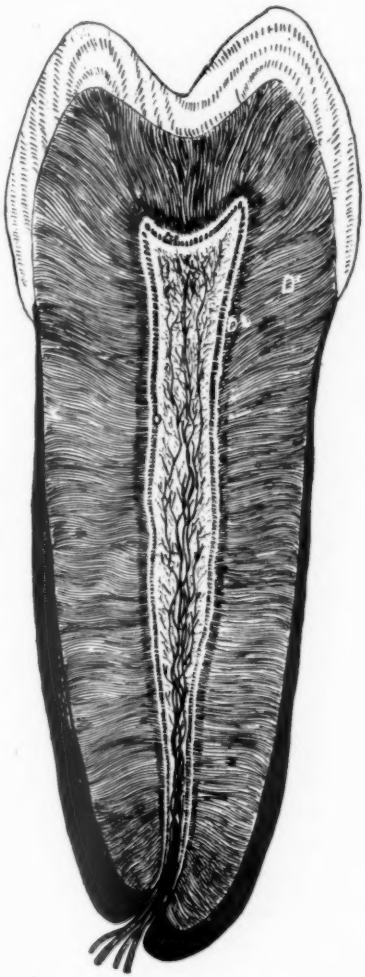

Fig. 1.—D^1, Primary dentine; D^2, secondary dentine; P_rD, predentine; O odontoblasts.

SECONDARY DENTINE

With the eruption of the teeth, and especially with occlusal contact, the pulp begins to receive the slight aggressive effects of normal biologic function (mastication, light thermal changes, chemical irritants, and slight traumas).

In my "pathogenic classification of pulp alterations," these aggressions are referred to as being of the first grade or order, since they are within the threshold of pulpal resistance and easily stimulate the defense mechanism of the pulp. In response, the pulp forms intermittent layers of secondary dentine (Figs. 1 and 2, D^2), referred to by other authors as compensating, protective, adventitious, senile, normal physiologic, tubular, typical, pathologic, physiopathologic, regular, regular-primary, neodentine, regular-secondary, irregular, normal-secondary, regular-physiologic, irregular dentine of the first order, of the second order, primary-odontoblastic, etc.

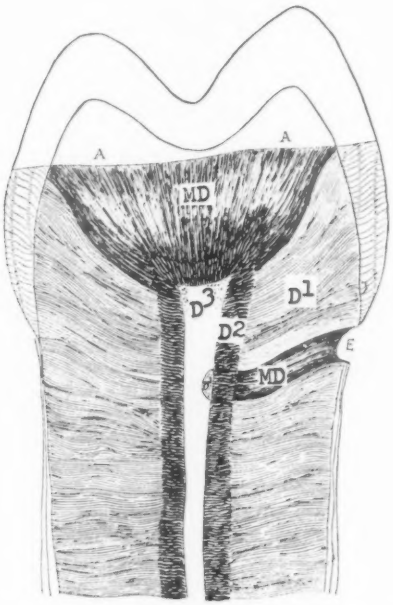

Fig. 2.—*A*, Abrasion; *E*, erosion; *MD*, dentinal metamorphosis; D^1, primary dentine; D^2, secondary dentine; D^3, tertiary dentine.

This secondary dentine is generally separated from the primary dentine by a line or demarcation zone which may or may not be very noticeable. It is less permeable and also has less dentinal tubules due to the reduction in the number of dentinoblasts per square millimeter and consequently in the number of Tomes' fibers. It is somewhat darker in color than the primary dentine, and its tubules are more curved, sometimes angulated, less regular, and smaller in diameter. This secondary dentine is deposited over the primary one for the purpose of better defending the pulp and reducing the size of the pulp cavity. However, the floor and the roof of the pulp chamber in premolars and molars usually receive more of this deposit.

TERTIARY DENTINE

When the pulp irritants are more intense or more aggressive (classified as second grade*) and almost reach the limit of pulp tolerance (abrasion, erosion, caries, dentinal exposure by fracture or during the preparation of cavities or crowns, improper medication, and harmful filling material), there is the formation of still another type of dentine which I refer to as tertiary dentine (Fig. 2, D^3). This has also been referred to by others as pathologic, protective, secondary, adventitious, reparatory, irregular, compensating, irregular-secondary, irregular of the third order, amorphous, irritational, physiopathologic, irregular-odontoplastic, etc.

This dentine differs from the aforementioned types as follows:

1. It is localized exclusively in front of the irritated zone.
2. The dentinal tubules are greatly irregular, even tortuous.
3. The tubules are reduced in number or are absent.
4. The calcification is deficient.
5. There are cellular inclusions which convert into spaces.
6. There is a tonality difference.

With this simple classification based on the characteristics of the three types of dentine (although there are probably more differences that may be found with the electronic microscope), it should be possible to eliminate much of the confusing terminology that exists in current dental literature.

REFERENCES

1. Alcayaga, O. C., and Olazabal, R. A.: Patología, Anatomía y Fisiología Patológica Bucodental, Buenos Aires, 1947, El Ateneo.
2. Bernick, S., Baker, R. F., Rutherford, R. L., and Warren, O.: Electron Microscopy of Enamel and Dentin, J. Am. Dent. A. **45**: 689-696, 1952.
3. Bernier, J. L.: The Management of Oral Disease, St. Louis, 1955, The C. V. Mosby Company.
4. Bevelander, G., and Benzer, S.: Morphology and Incidence of Secondary Dentin in Human Teeth, J. Am. Dent. A. **30**: 1075-1082, 1943.
5. Beust, T. B.: Posteruptive Changes in Maturation of Teeth, J. Am. Dent. A. **18**: 2186-2192, 1931.
6. Bodecker, C. F.: Fundamentals of Dental Histology and Embryology Including Clinical Applications, New York, 1944, Columbia University Press.
7. Cabrini, R.: Histología y Embriología buco-dentaria, Buenos Aires, 1947, El Ateneo.
8. Duncker, G.: Das morphische Altern der Pulpa des Zahnes, Deutsche. Zahn. Ztschr. **7**: 1428-1432, 1952.
9. Erausquin, J.: Histología Dentária Humana, Buenos Aires, 1953, Progrental.
10. Feldman, G. L., and Feldman, P. I.: Plasticheskaya deyatelnost pulpii, Sovet. stomatol. **4**: 21-39, 1934.
11. Feldman, G. L., and Feldman, P. I.: Revisia nekotoriij poloshenivy v uchenii o biologuii pulpi, Sovet. stomatol. **4**: 7-21, 1934.
12. Filgueiras, J., and Mello, C.: Patologia Da Polpa Dentária, ed. 3, Rio de Janeiro, 1955, Cientifica.
13. Fischer, G.: Das morphische Altern der Pulpa des Zahnes, Deutsche Zahn. Ztschr. **8**: 424-426, 1953.
14. Fischer, G.: Biologie der Pulpa des Menschlichen Zahnes, Leipzig, 1955, Johann Ambrosius Barth.

*The third grade produces light pathologic alterations of the pulp, and the fourth produces definite pathologic destruction of the same pulp.

15. Fuentes, A.: Algunas consideraciones morfológicas sobre los canalículos dentinarios, An. Fac. odont. Montevideo **11**: 105-121, 1956.
16. Glickman, I., and Shklar, G.: Effect of Systemic Disturbances on the Pulp of Experimental Animals, ORAL SURG., ORAL MED. & ORAL PATH. **7**: 550-558, 1954.
17. Hill, T. J.: Pathology of the Dental Pulp, J. Am. Dent. A. **21**: 820-844, 1934.
18. Ireland, R. L.: Secondary Dentin Formation in the Deciduous Teeth, J. Am. Dent. A. **28**: 1626-1632, 1941.
19. Kamrin, B. B.: The Dental Pulp, D. Digest **40**: 48-51, 1934.
20. Kantorowicz, A.: Odontología Conservadora, Barcelona, 1937, Ed. Labor S. A.
21. Kennedy, J. J., Teuscher, G. W., and Fosdick, L. S.: The Ultramicroscopic Structure of Enamel and Dentin, J. Am. Dent. A. **46**: 423-431, 1953.
22. Kronfeld, R.: Histopathology of the Teeth, Philadelphia, 1949, Lea & Febiger.
23. Kuttler, Y.: Microscopic Investigation of Root Apexes, J. Am. Dent. A. **50**: 544-552, 1955. (Also Bol. odont. mexicano, pp. 2-16, 1955; Gaceta odont. Venezuela, pp. 97-111, 1955; Prótesis Clínica Habana, pp. 3-8, 1956.)
24. Kuttler, Y.: Caries dentinaria profunda, Prótesis Clínica (Habana), pp. 6-8, 10-12, 14, 1958.
25. Kuttler, Y.: Alteraciones pulpares en general, Rev. Asoc. odont. argent. 399-403, 1958.
26. Kuttler, Y.: Pulpitis en general, Rev. odont. Costa Rica **1**: 11-15, 1958.
27. Lukomsky, I. G.: Terapevticheskaya Stomatologuia, Moskwa, 1955, Medguis.
28. Manley, E. B.: Some Observations on the Defense Mechanism of the Dental Pulp, D. Gaz. **14**: 31-34, 1947.
29. Manley, E. B., Brain, E. B., and Marsland, E. A.: An Atlas of Dental Histology, ed. 2, Oxford, 1955, Blackwell Scientific Publications.
30. Maximow, A. A., and Bloom, W.: Tratado de Histología, ed. 3, Buenos Aires, 1952, Ed. Labor S. A.
31. Meyer, W.: Anatomia en el Tratado de Odontología de Port-Euler, Barcelona, 1943, Ed. Labor S. A.
32. Muller, O.: Pulpa und wurzelbehandlung, Basel, 1953, Benno Schwabe.
33. Noyes, F. B.: Oral Histology and Embryology, ed. 7 (revised by I. Schour), Philadelphia, 1953, Lea & Febiger.
34. Orban, B.: Oral Histology and Embryology, St. Louis, 1944, The C. V. Mosby Company.
35. Palazzi, S.: Aspects histologiques de l'atrophie de la pulpe, Rev. franç. d'odonto-stomatol. **2**: 559-564, 1955.
36. Palazzi, S.: Trattato di Odontologia, Milano, 1950, Ulrico Hoepli.
37. Palazzi, S.: Contribution systématique aux études sur la biologie de la pulpe et aux recherches sur les pulpopathies métastasiques hématogenes et constitutionnelles, L'Odontologie **72**: 713-716, 1934.
38. Pincus, P.: Some Physiological Data on the Human Dental Pulp, Brit. D. J. **89**: 143-148, 1950.
39. Pucci, F. M., and Reig, R.: Conductos Radiculares (la Parte), Montevideo, 1944, Barreiro y Ramos.
40. Scott, D. B.: Recent Contributions in Dental Histology by Use of the Electron Microscope, Internat. D. J. **4**: 64-95, 1953.
41. Shroff, F.: Thoughts on the Physiologic Pathology of Regressive and Reparative Changes in the Dentine and Dental Pulp, ORAL SURG., ORAL MED. & ORAL PATH. **5**: 51-58, 1952.
42. Shroff, F. R., Williamson, K. I., and Bertaud, W. S.: Electron Microscope Studies of Dentin, ORAL SURG., ORAL MED. & ORAL PATH. **7**: 662-670, 1954.
43. Shroff, F. R., Williamson, K. I., Bertaud, W. S., and Hall, D. M.: Further Electron Microscope Studies of Dentine, ORAL SURG., ORAL MED. & ORAL PATH. **9**: 432-443, 1956.
44. Sicher, H.: Biology of the Dentin, Bur **46**: 121-127, 1946.
45. Sicher, H.: Biology of Attrition, ORAL SURG., ORAL MED. & ORAL PATH. **6**: 406-412, 1953.
46. Starobinsky, I. M.: Stomatologuia, ed. 2, Moskwa, 1951, Medguis.
47. Stones, H. H.: Oral and Dental Diseases, ed. 3, Edinburgh, 1954, E. & S. Livingstone.
48. Symons, N. B. B.: Development of the Fibres of the Dentine Matrix, Brit. D. J. **101**: 255-262, 1956.
49. Takuma, S.: Electron Microscopy of Dental Tissues by Use of the Replica Method, D. Abst. **2**: 399-400, 1957.
50. Thomas, B. O. A.: "Gerodontology," the Study of Changes in Oral Tissues Associated With Aging, J. Am. Dent. A. **33**: 207-213, 1946.
51. Turell, J. C., and Costas, J. B.: Estudio de a Dentina de compensación, Odont. Uruguaya, pp. 411-440, 1954.
52. Vorobiev, B., and Piett, E. K.: Osnovi anatomii, guistologii y embriologii subov y polosti rta, Berlin, 1922, Vrach.
53. Walkhoff, O., and Hess, W.: Lehrbuch der Konservierenden Zahnheilkunde, ed. 5, Leipzig, 1954, Johann Ambrosius Barth.

54. Weider F. R., Schour, I., and Mohamed, C. I.: Reparative Dentin Following Cavity Preparation and Fillings in the Rat Molars, ORAL SURG., ORAL MED. & ORAL PATH. 9: 221-232, 1956.
55. Willman, W.: Calcifications in the Pulp, Bur 34: 73-76, 1934.
56. Zander, H. A.: Physiology of the Dental Pulp, Queensland D. J., pp. 33-37, 1953-1954.
57. Zerosi, C.: Terapia Conservativa in Odonto-Stomatologia, Torino, 1955, Edizioni Minerva medica.

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RESEARCH

A DIVERGENT APPROACH TO TOOTH BUD TRANSPLANTATION

Leon Herschfus, D.D.S., Detroit, Mich.*

IN A preliminary study[1] the results of an experiment in the transplantation of tooth buds in dogs were reported.

After reviewing the failures of tooth bud transplantation in the dog, it has been decided to approach the problem from a different position. Loeb[2] has theorized that the success of any transplant is determined largely by the "individuality differentials" that arise between the recipient host and the donor

Fig. 1.—Incision for cesarean section.

Received for publication July, 1958.

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transplant. Thus, an immune response develops instantaneously upon organic union of host and transplanted bud. It would appear that this hypothesis would account for our failures in so far as our transplanted tooth buds were undergoing differentiation, with tissue specificity already being established, when they were secured in the host tissue. Of course, other factors could have influenced the survival of the transplant.

Fig. 2.

Fig. 3.

Fig. 2.—A litter of five rabbits, showing the five placental buds. In each bud is a baby rabbit.

Fig. 3.—Fetus (rabbit) being delivered from a placental bud.

To test this "immunity hypothesis" or "biologic individuality," however, we are now approaching the problem from two different angles.

In one group we are now transplanting the buds from rabbit and puppy embryos in the first half of the gestation period when individuality differentials

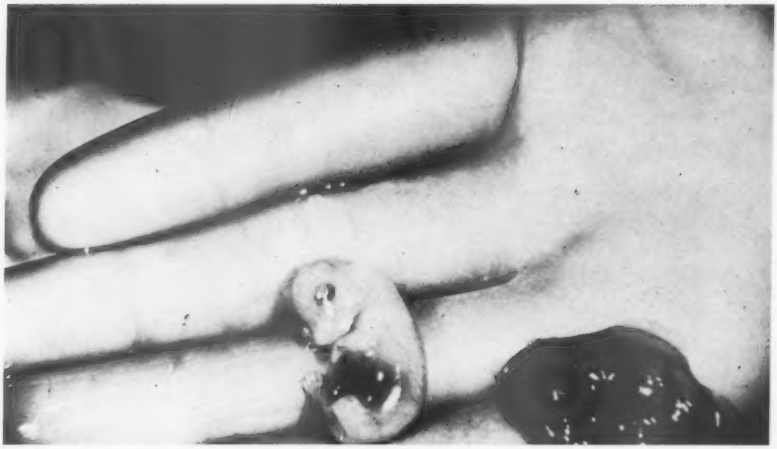

Fig. 4.—Rabbit fetus in Fig. 3 after delivery.

Fig. 5.—Insertion of bud from rabbit embryo into buccal fold of mother rabbit.

Fig. 6.

Fig. 7.

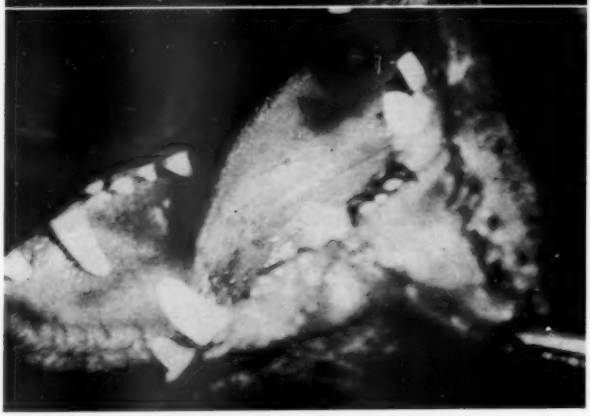

Fig. 8.

Fig. 6.—Extracted molar with prepared socket to receive the bud.
Fig. 7.—Buccal and lingual flaps laid back and bud ready to be inserted.
Fig. 8.—Suturing completed.

and immune responses should be at a minimum. The buds are inserted either in the socket of a freshly extracted tooth or in the mucobuccal fold for better vascularization (Figs. 1 to 10).

In our second group, in order to overcome the destructive action of the host's enzymes, we are first "conditioning" the recipient hosts by direct blood vessel union between host and donors (vascular parabiosis). In the hope that

Fig. 9.

Fig. 10.

Fig. 9.—Bud ready to be inserted in mucobuccal fold (dog).
Fig. 10.—Suturing completed.

the recipient host will be conditioned to "accept" the donor transplant, this is repeated several times with different donors before the buds are finally transplanted.

We are hoping to translate this work to man, using tooth buds of human embryos obtained from spontaneous abortions or stillbirths. If this should prove

successful, a major breakthrough would be achieved and homologous transplants in man would eventually become a reality.

The author wishes to express his appreciation to Dr. J. W. Pichette, Chief of the O.B. Department, Mt. Carmel Mercy Hospital, and his staff for the full cooperation received.

REFERENCES

1. Herschfus, L.: Transplantation of Toothbuds in Dogs, D. Digest **63**: 62-64, 1957.
2. Loeb, Leo: The Biological Basis of Individuality, ed. 1, Springfield, Ill., 1945, Charles C Thomas, p. 161.

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Section by the

ARMED FORCES AND PUBLIC HEALTH SERVICE

SPINDLE-CELL SQUAMOUS CARCINOMA OF THE LIP

Report of Four Cases

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Washington, D. C.

SPINDLE-CELL carcinoma is a unique and rare tumor found in various regions of the body. Willis[6] reported examples in the tongue, parotid, bronchus, and cervix. In a generic sense, it is grouped with undifferentiated or anaplastic carcinomas. However, due to its consistent spindle-cell pattern, expansile type of growth, initial small size, and frequent association with irradiation or trauma, it deserves special consideration as an entity.

The histogenesis of this tumor is indeed controversial, since the spindle-cell feature is often difficult to differentiate from sarcomatous lesions. In some instances the diagnosis is a matter of interpretation by the reviewing pathologist.

Spindle-cell carcinoma should not be confused with lesions associated with thermal burn scars. Carcinomas which develop in deep-seated burn scars are usually of the squamous-cell type, whereas those in more superficial scars are usually of the basal-cell variety. Spindle-cell features are rare in either.

All oral cases in the files of the Armed Forces Institute of Pathology which had been diagnosed as undifferentiated, anaplastic, and spindle-cell carcinoma were reviewed. Four cases in which the tumor was located on the lip were selected. The selection was based on the fact that the lesions (1) were initially less than 1 cm. in diameter, (2) had a dominant spindle-cell configuration, and (3) were difficult to identify as epithelial in origin due to their sarcomatous appearance.

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Martin and Stewart[1] described eight cases of spindle-cell epidermoid carcinoma. Seven were in the oral region, and of these four were located on the lip. De Cholnoky[4] described four cases of round, spindle, and neurogenic sarcomas of the lip, and three of his cases were histologically consistent with spindle-cell carcinoma. Goldman and Grady[2] reported a single case on the lip.

Martin and Stewart noted a relationship between roentgen irradiation, particularly when combined with cautery or endothermy, and the development of these peculiar spindle-cell carcinomas. In none of their cases was a thermal burn responsible for the scarring in the area in which carcinoma of this kind developed. In Goldman and Grady's case, however, the spindle-cell carcinoma arose at the site of an initial lesion which resulted from a burn from the lighted end of a cigar. Of de Cholnoky's three cases, one was associated with a burn on the lip caused by hydrochloric acid and 2 had no history of radiation or trauma. These two cases and three of the four cases that we have to report were similar in that none were preceded by roentgen therapy or trauma. In our Case 3 an unidentified liquid medication was applied to the lip for six weeks and may have influenced the clinical course.

CASE REPORTS

CASE 1 (AFIP ACCESSION 626480).—In December, 1953, a 53-year-old white man noted that a lesion on his lower lip had recently increased in size. It was indurated, with a central area of ulceration, and appeared to be squamous-cell carcinoma. There was no history of irradiation or trauma. The lesion was excised.

Histologically, the surface of the lesion was ulcerated. The tumor cells which invaded deep into the underlying muscle had well-defined oval to spindle-shaped nuclei as well as acidophilic, and at times vacuolated, cytoplasm. These cells were grouped in strands and bundles, which formed a whorled pattern. Intimately admixed with the tumor cells were chronic inflammatory elements, principally lymphocytes. Deep in the section the tumor cells invaded striated muscle, causing degeneration and fibrosis (Figs. 1 and 2).

CASE 2 (AFIP ACCESSION 694898).—A 52-year-old white man had noticed a lesion on the vermilion border of the lower lip for the past five months. The lesion, which was painless, measured approximately 0.5 cm. in its greatest diameter.

Histologically, the surface of the lesion was ulcerated and covered by a fibrinous exudate (Fig. 3). The tumor cells, which were arranged in whorls, had large hyperchromatic, oval or spindle-shaped nuclei with clumping of chromatin in some instances. Formation of tumor giant cells was also noted. The tumor cells had a sarcomatoid appearance, but the nuclear formation and over-all pattern of growth were characteristic of spindle-cell carcinoma.

CASE 3 (AFIP ACCESSION 758642).—A 39-year-old white man had a small lesion on the lower left side of the lip which was treated with a liquid medication for six weeks but did not heal. The patient was referred to the hospital, and on three occasions in the past year biopsy of the lesion was performed.

The histologic report in every instance was ulceration with acute and chronic inflammation. Seven months after the last biopsy the patient returned to the hospital with a recurrence of the ulceration of the lip. The lesion was about 0.5 cm. in diameter and slightly tender. It was excised, and a diagnosis of leukoplakia was made. Nine months

Fig. 1.—Case 1 (AFIP Accession 626480). The tumor is well demarcated. To the left of the arrows is tumor tissue, with striated muscle tissue of the lip to the right. (Hematoxylin and eosin stain. Magnification, ×7½; reduced ⅙.)

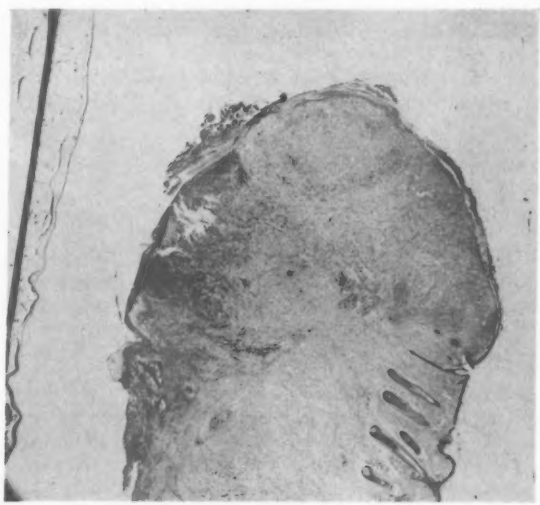

Fig. 2.—Case 3 (AFIP Accession 758642). The topography of the tumors is almost identical to that of Case 1. (Hematoxylin and eosin stain. Magnification, ×7½; reduced ⅙.)

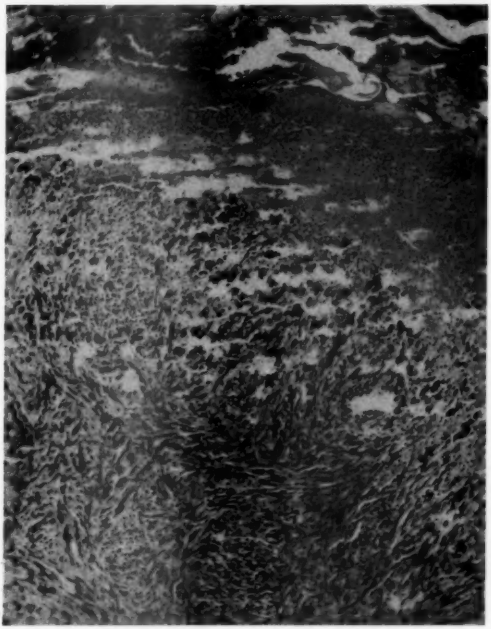

Fig. 3.—Case 2 (AFIP Accession 694898). The ulcerated surface and covering exudate are characteristic of all four lesions. (Hematoxylin and eosin stain. Magnification, ×115; reduced ⅙.)

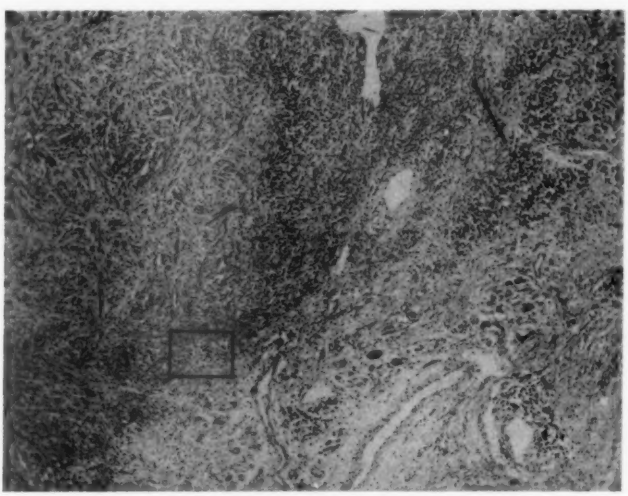

Fig. 4.—Case 1 (AFIP Accession 626480). Demarcation of tumor above from underlying muscle. (Hematoxylin and eosin stain. Magnification, ×50; reduced ⅙.)

later the patient returned with a recurrent lip lesion. Biopsy report at this time was spindle-cell carcinoma of the lip. Partial mandibulectomy and radical neck dissection of the left side were performed. No evidence of tumor was found on microscopic examination of the mandible and lymph nodes.

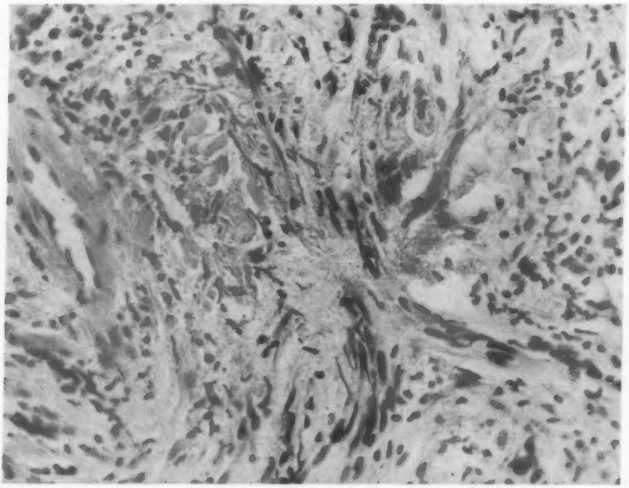

Fig. 5.—Case 1. (AFIP Accession 626480). Blocked area of Fig. 4, showing peculiar fibrosis at junction of tumor and underlying muscle bundles.

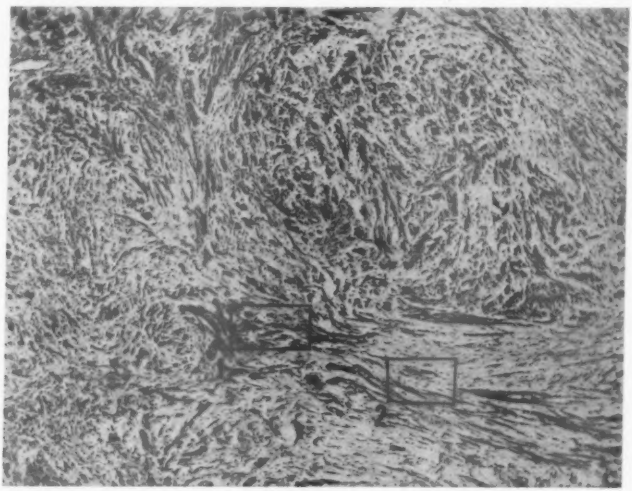

Fig. 6.—Case 3 (AFIP Accession 758642). Clusters of epithelial cells assuming a spindle appearance. (Hematoxylin and eosin stain. Magnification, ×50; reduced ⅙.)

Histologic examination of a wedge section of lip revealed that part of the surface was ulcerated and covered with a fibrinous exudate; the intact surface was covered by

stratified squamous epithelium. The underlying connective tissue was invaded by strands of spindle-shaped cells, and in several areas the whorled pattern gave the well-defined margin so characteristic of these lesions.

The cells could readily be identified as epithelial in one area, and from there they spindled out to resemble the bulk of the lesion. Deeper in the section, cells invaded the striated muscle. Mitotic activity, pleomorphism, and hyperchromatism were marked, particularly where the cells were arranged in clusters. The epithelial background of this tumor was most convincing.

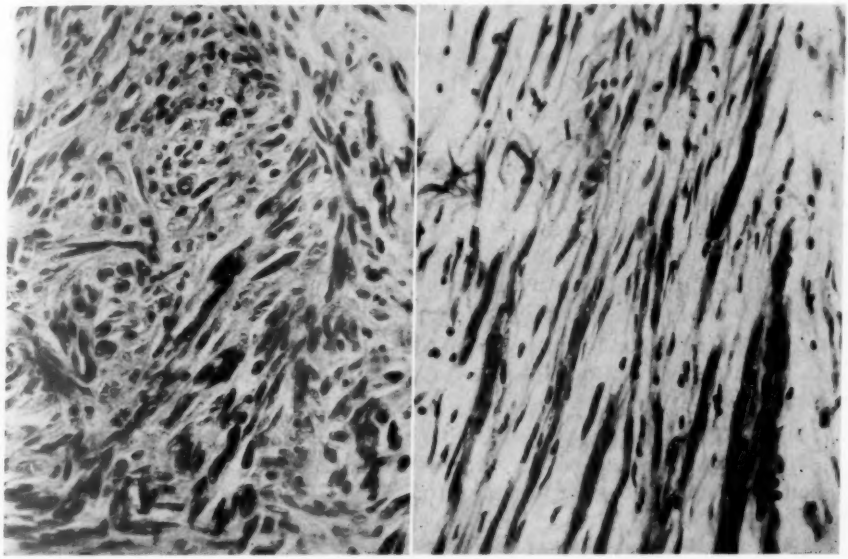

Fig. 7. Fig. 8.

Fig. 7.—Case 3 (AFIP Accession 758642). Blocked area *1* from Fig. 6. Epithelial cells transformed into a spindle shape. (Hematoxylin and eosin stain. Magnification, ×305; reduced ¼.)

Fig. 8.—Case 3 (AFIP Accession 758642). Blocked area *2* from Fig. 6. Epithelial cells in a more pronounced spindle configuration.

Case 4 (AFIP Accession 814972).—A 44-year-old white man had a keratotic lesion of two or three months' duration on the lower lip. It was "hornlike" in appearance and was located on the vermilion border. The lesion was excised.

Microscopic examination revealed a lesion covered by stratified squamous epithelium with an area of ulceration. The epithelial cells of the rete ridges spindled out and invaded deep into the underlying connective tissue and muscle, as in the preceding cases.

DISCUSSION

The tumors that we are reporting are decidedly different from anaplastic or undifferentiated carcinoma of the lip in that the cells, although undifferentiated, were uniformly spindle-shaped. The tumors were initially small, less than 1 cm. in diameter, and they were well demarcated from the underlying connective tissue and muscle. They formed a compact mass which appeared to grow in an expansile manner rather than by the fingerlike pro-

jections characteristic of undifferentiated carcinoma (Figs. 4 and 5). Since the spindle-cell pattern has been observed in numerous tumors of different histogenetic backgrounds, it was important to determine whether those in question were epithelial or mesenchymal in origin.

An attempt was made to demonstrate the histogenetic background of these tumors by means of differential stains, even though it was realized that these would be greatly limited in application because of the lack of differentiation in these tumors. Furthermore, in many instances identification as to origin of spindle-cell tumors is a matter of interpretation. However, Masson's and Wilder's reticulum stains were used in an effort to shed light on the origin of these cells. The Wilder reticulum stain was inconsistent and therefore not particularly helpful. In undifferentiated epithelial tumors the distribution of reticulum fibers is often suggestive of mesenchymal tumors (for example, lymphoepithelioma of the nasopharynx).

The Masson stain suggested that the spindle cells were of epithelial origin, since they were producing little or no collagen. However, collagen fibers are rarely observed in undifferentiated mesenchymal tumors; hence, differentiation between tumors of epithelial and mesenchymal origin by differential stains was not satisfactory.

The morphologic features and the direct continuity of the spindle cells with the overlying epithelium in serial sections (Figs. 6, 7, and 8) were considered the best evidence for identifying some spindle-cell tumors as being of epithelial origin.

The cases reviewed in the literature which were most like ours in regard to location and histologic features were the four lip lesions reported by Martin and Stewart,[1] three of four cases reported by de Cholnoky,[4] and the single case of Goldman and Grady.[2] An interesting observation was made concerning these reported cases and ours. In the four cases presented by Martin and Stewart the history of trauma to the lip was consistent—radiation, endothermy, or cautery in three cases and physical trauma in one case. In three of these, the patients died with metastases, and in the fourth, after several operations, the patient refused further treatment although he had evidence of the disease but no metastases after four years. Goldman and Grady's patient died approximately eighteen months after removal of the initial lip lesion which was preceded by a thermal burn. At the time of their report the patient was alive and apparently without metastasis, but eventually he died as a result of local extension into the submandibular and neck tissues.

Of de Cholnoky's four cases, which were reported as round, spindle and neurogenic sarcomas of the lip, his Case 1, although the tumor was on the lip, was not histologically compatible with this group of cases. The remaining three were strikingly similar to this group, and in his second case the history was that the lip had been burned with hydrochloric acid and had never healed. Radical removal of the lesion was followed by bilateral neck dissection. The diagnosis was equivocal between neurogenic sarcoma and a

tumor of epithelial origin. Unfortunately, the patient was lost to follow-up six months after treatment; hence, the clinical course was not evaluated. In de Cholnoky's last two cases there was no history of trauma or radiation, and the lesions were excised along with node dissections of the affected side. The nodes were negative for tumor, and there was no evidence of local or regional recurrence after four years, in Case 3, and eight months, in Case 4.

These last two cases of de Cholnoky were similar to the four that we reported in that they were located on the lip. There was no previous history of radiation or trauma in our cases, except the unidentified liquid medication applied for six weeks in our Case 3, and histologically the tumors had a spindle-cell appearance. It was interesting to observe that there was no history of recurrence or metastases in any of the cases in which there was no previous history of radiation or trauma. This was in striking contrast to the four cases reported by Martin and Stewart and to Goldman and Grady's report in which there was a history of radiation or trauma and metastases or repeated recurrences.

The clinical course may have been influenced in de Cholnoky's second case by chemical trauma to the lip and in our Case 3 by treatment for six weeks with an unknown liquid medication. Although diagnosis was questionable, the clinical history alone may warrant the inclusion of these cases in the same group with those reported by Martin and Stewart and Goldman and Grady.

In reviewing our four cases, the morphologic features substantiated the belief that some spindle-cell tumors were of epithelial origin. This was particularly well demonstrated in Case 3, in which a cluster of epithelial cells was observed transforming into spindle cells. Although the number of cases involved was small, it appeared that the history of radiation or trauma may alter the clinical course of apparently identical lesions.

In the oral regions, spindle-cell tumors of epithelial origin have been observed in association with (1) irradiation, (2) thermal burns, and (3) no history of trauma. The histologic features of our four cases appear to be identical to the cases in which a history of trauma was associated. Although follow-up data were inadequate in our cases, there was no history of recurrence following initial surgical removal except in Case 3. The follow-up on our Case 1 was at the four-year interval, in Cases 2 and 3 after two and one-half years, and in Case 4 after six months. Goldman and Grady's case was reviewed and was identical, histologically, to our cases. The clinical course of their patient was essentially similar to Martin and Stewart's, however, in that death resulted from the lesion.

The presence or absence of previous radiation or trauma may influence the clinical course of spindle-cell carcinoma of the lip. The prognosis of spindle-cell carcinoma of the lip preceded by radiation or trauma was extremely poor, while in those cases without such a previous history the prognosis appeared to be more optimistic.

SUMMARY

Four original cases of spindle-cell squamous carcinoma of the lower lip are reported. Three of these cases were not associated with previous irradiation, thermal burn, or trauma. One was treated with an unknown liquid medication, and in this case there were several recurrences.

Clinically, all the lesions were less than 1 cm. in diameter and were of less than six months' duration. Histologically, all the lesions appeared well delineated; each showed surface ulceration and uniform spindle-cell structure.

In previously reported cases of spindle-cell carcinoma of the lip associated with irradiation, thermal burn, or trauma, prognosis was grave. In cases without a previous history of irradiation, thermal burn, or trauma, the prognosis appeared to be good.

REFERENCES

1. Martin, H. E., and Stewart, F. W.: Spindle Cell Epidermoid Carcinoma, Am. J. Cancer **24**: 273-298, 1935.
2. Goldman, H. M., and Grady, H. G.: Case Reports From the Army Institute of Pathology, Am. J. Orthodontics & Oral Surg. **31**: 189-196, 1945.
3. Treves, N., and Pack, G. T.: The Development of Cancer in Burn Scars, Surg. Gynec. & Obst. **51**: 749-782, 1930.
4. De Cholnoky, T.: Round-Cell, Spindle-Cell, and Neurogenic Sarcomas of the Lip, Am. J. Cancer **22**: 548-554, 1934.
5. Ewing, J.: Neoplastic Diseases, ed. 4, Philadelphia, 1940, W. B. Saunders Company.
6. Willis, R. A.: Pathology of Tumors, St. Louis, 1948, The C. V. Mosby Company.
7. Reinhard, M. C., Thibaudeau, A. A., and Candee, C. F.: The Development of Multiple Tumors in Tarred and Radiated Mice. Part II, Am. J. Cancer **22**: 590-596, 1934.
8. Rusch, H. P.: Carcinogenesis: A Facet of Living Processes, Cancer Research **14**: 407-417, 1954.
9. Berenblum, I.: A Speculative Review: The Probable Nature of Promoting Action and Its Significance in the Understanding of the Mechanism of Carcinogenesis, Cancer Research **14**: 471-477, 1954.
10. Rigdon, R. H., and Brashear, D.: Experimental Production of Squamous-Cell Carcinomas in the Skin of Chickens, Cancer Research **14**: 629-631, 1954.
11. Levy, B., and Ring., J. R.: The Experimental Production of Jaw Tumors in Hamsters, ORAL SURG., ORAL MED. & ORAL PATH. **3**: 262-271, 1950.

HYPEROSTOSIS OF THE MANDIBLE

Report of a Case

Harold G. Green, Captain (DC) USN

FIBRO-OSSEOUS lesions of the bone have accumulated a multitude of synonyms because of their varying clinical manifestations, roentgenographic findings, and theories of etiology. An unusual case, in which the basic picture is one of reactive bone and fibrous tissue proliferation, is reported here.

History.—In June, 1954, a 22-year-old hospitalman, USN (Fig. 1), first noticed a lump on his left jaw. Examination at that time elicited the diagnosis of osteoma of the mandible, and the patient was advised to seek aid if the lesion enlarged. On Nov. 4, 1955, the patient was admitted to the hospital for evaluation and treatment of the lesion, since it was felt that the tumor was enlarging.

Past history revealed that the patient had been a pipe fitter in a steel mill before entering the service. He played high school and semiprofessional football, during which time his jaw was struck on different occasions.

Family history revealed that his paternal grandfather had tuberculosis and his maternal grandfather died of Hodgkin's disease. A left parotid tumor was removed in March, 1953. Systemic review showed that the patient had always been in good health. He denied having a cough, although there was occasional pectoral pain.

Physical examination revealed an essentially normal male patient. The head and neck, except for asymmetry of the left face, appeared to be normal. There was a hard, nontender, ovoid enlargement of the left anterior body of the mandible. There were no palpable lymph nodes in the face or neck, and there was no pigmentation of the overlying skin. There was full mandibular movement. Eyes, ears, and nose were essentially negative. In the mouth, the oral mucosa was intact. The teeth were in good repair; they were not sensitive to percussion and gave normal response to thermal changes, and normal dental occlusion was present. The buccal and lingual alveolus of the left mandible was enlarged over the right, particularly in the area of the lower left first molar. There was no evidence of endocrine disturbance.

Roentgenographic examination showed the chest to be normal. Oblique-lateral films of the mandible revealed a rounded density in the left body, which appeared as an osteomatous thickening (Figs. 2 and 3). Periapical views of the left mandible showed an expanding lesion with concentric lamination of the bone. There was a 1 cm. growth enveloping and apparently causing resorption of the mesial root of the lower left first molar (Fig. 4). A bone survey, which included the skull, entire spine, pelvis, and hip, revealed no pathologic condition of the bones or joints. The results of laboratory procedures, including urinalysis, hematology, and determinations of inorganic phosphorus and calcium, were within normal limits.

From the United States Naval Hospital, Camp Pendleton, California.

A biopsy of the bony lesion revealed it to be composed of parallel bands of dense bony trabeculae, appearing quite regular and well formed and averaging 150 microns in width. The fibrous tissue was composed of typical spindle-cell nuclei and was moderately cellular. Relatively few blood vessels were seen. The portion of the specimen corresponding to the cortex showed no significant difference from the remainder of the tissue.

The basic picture was one of reactive bone and fibrous tissue proliferation. In view of the clinical course, a diagnosis of nonspecific hyperostosis was made.

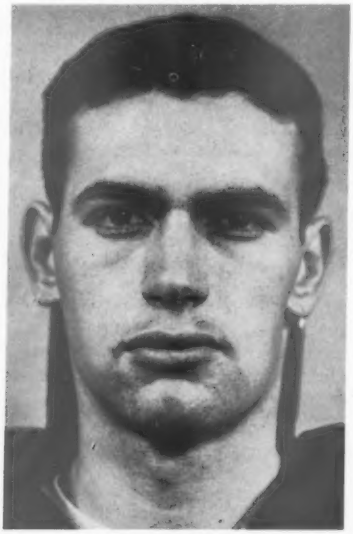

Fig. 1.—Photograph showing enlargement of left mandible.

Evaluation six months later revealed that the biopsy wound had healed normally and that the bony tumor was approximately the same size and condition as upon initial examination. No treatment was advised, for it was felt that the lesion was self-limiting. It was nonsymptomatic and did not interfere with function, and the patient was not concerned with the slight asymmetry.

DISCUSSION

The varying findings of the different osseous lesions as well as the vague etiology surrounding them may be of some interest. Fibro-osteoma is a benign tumor originating in the spongiosa of bone in which there is a preponderance of fibrous to osseous tissues as well as varying degrees of calcification. This lesion has been variously classified as ossifying fibroma, osteofibroma, fibrous osteoma, and monostotic fibrous dysplasia (Fig. 5). Thoma[1] quotes Waldron as stating that it is a mistake to assume that all fibro-osseous lesions are identical or that they should be classified under one heading. He agrees with Pindborg (1951) that sharply circumscribed lesions may be properly considered as neoplasms, but if the bone is diffusely involved or if multiple lesions are present

Fig. 2.

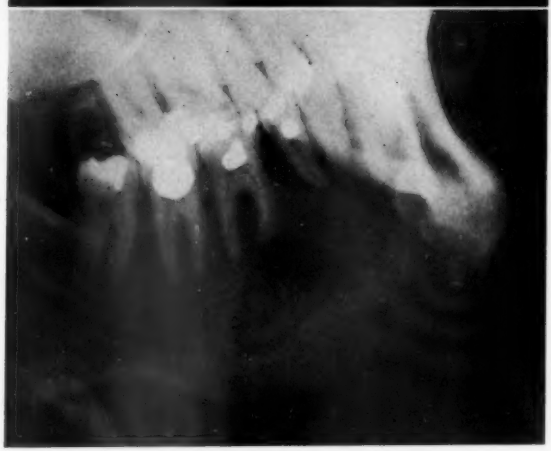

Fig. 3.

Fig. 2.—Anteroposterior roentgenogram. Note asymmetry of mandible.
Fig. 3.—Oblique-lateral view of left mandible.

Fig. 4.—Periapical view showing ground-glass appearance and peculiar growth around resorbing mesial root of first molar.

a neoplastic designation is not in keeping with established concepts of neoplasia and such cases should be diagnosed as fibrous dysplasia.

Fibrous dysplasia (Fig. 6) is generally accepted as a separate entity, distinct from generalized osteitis fibrosa cystica and from osteitis deformans. The cause of this disease is unknown. The hypothesis has been advanced that it is

Fig. 5.

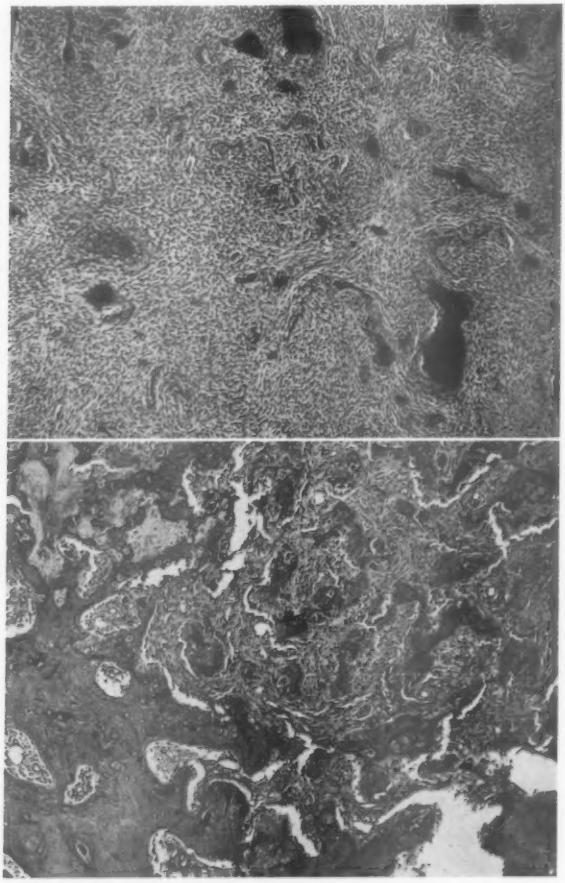

Fig. 6.

Fig. 5.—Photomicrograph of section from ossifying fibroma.
Fig. 6.—Photomicrograph of section from fibrous dysplasia.

a skeletal developmental anomaly resulting apparently from abnormal activity of the specific bone-forming mesenchyme. Abnormal response to injury has also been advanced as an etiological factor. The consensus that the monostotic

form is separate from the polystotic form seems to prevail. Thoma[2] feels that the term "monostotic" should apply only to the mandible, while Robinson[3] points out the advantages of the term "osseous dysplasia."

An osteoma may be made up of medullary or cortical bone. It is a benign, slow-growing tumor which arises from preformed bone and is believed to be

Fig. 7.

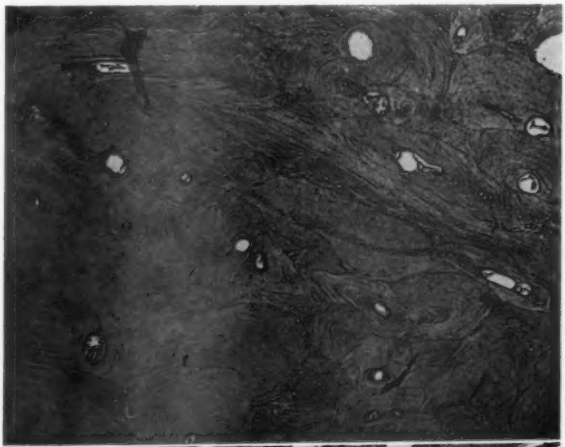

Fig. 8.

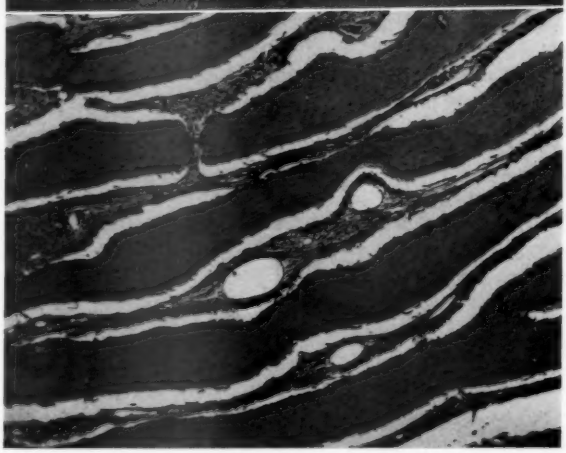

Fig. 7.—Photomicrograph of section from osteoma.
Fig. 8.—Photomicrograph of section from hyperostosis. Note orderly arrangement of fibrous and osseous tissue.

of traumatic origin. The cortical type (Fig. 7) shows compact bone throughout, with little fibrous stroma. In the case of hyperostosis presented it would seem that there are a number of similarities, both microscopically (Fig. 8) and

clinically. However, there does not appear to be any universal agreement as to etiology or classification of these lesions. Of clinical significance is the opinion that encapsulated lesions may be considered neoplasms and can be removed in toto, while the osseous dysplasias have no definite boundaries and their treatment has to be governed by the severity of symptoms, interference with function, and degree of disfigurement.

CONCLUSION

Attempting to classify reparative change in otherwise normal bone, such as seen in these mixed fibro-osseous lesions, presents a histologic challenge. From the clinician's viewpoint, however, this seems to be of only academic importance as he is faced with determining what treatment procedures, if any, should be instituted. The many descriptive terms given to these lesions of obscure etiology have tended to confuse treatment planning.

Primary responsibility lies in first ruling out neoplastic disease, in which early and vigorous care is indicated. Second, an exhaustive search for systemic etiological factors will rule out the possibility of these lesions being an oral manifestation of some general disease. Despite such study, final determination is very often inconclusive, but only after study to this point can a more leisurely approach to definitive treatment be made.

Contemporary practice calls for the nonsurgical approach to these problems of abnormal reparative change of jawbones that are otherwise normal. When the enlargement is cosmetically objectionable, however, it can be surgically contoured to more acceptable proportions. Hyperostosis is a very slow-growing lesion with no known morbid potential. It should be anticipated that subtotal surgery, such as may be done for cosmetic reasons, will not delay the progressive nature of the problem.

REFERENCES

1. Thoma, Kurt H.: Oral Pathology, ed. 4, St. Louis, 1954, The C. V. Mosby Company, p. 1274.
2. Thoma, Kurt H.: Oral Pathology, ed. 4, St. Louis, 1954, The C. V. Mosby Company, p. 768.
3. Robinson, Hamilton B. G.: Osseous Dysplasia, J. Oral Surg. 14: 5, 1956.

ANNOUNCEMENTS

American Academy of Oral Pathology

The following is a brief résumé of the papers presented at the Academy's thirteenth annual meeting in Minneapolis, Minnesota, April 17 to 19, 1959. The papers will be published in a later issue of the JOURNAL.

1. MORE UNUSUAL ORAL SYNDROMES. Robert J. Gorlin.

(A group of seven unusual syndromes, including Pierre-Robin syndrome, Pringle-Bourneville syndrome, and Keppel-Feil syndrome, were presented and the characteristics of each were demonstrated.)

2. FORMATION OF ENAMEL IN AMELOBLASTOMA. Victor Kalnins and Paul E. Boyle.

(Development of enamel has been recognized in odontogenic tumors which contain dentine but not in the ameloblastoma. The authors' findings indicate that ameloblastomas can produce young transitional enamel matrix in droplet form in the advanced neoplasm.)

3. MULTIPLE MALIGNANT TUMORS INVOLVING THE ORAL MUCOSA AND GASTROINTESTINAL TRACT. Irving Meyer and Gerald Shklar.

(Forty-eight cases of multiple malignant tumors involving the oral mucosa were studied in four female and forty-four male patients aged 39 to 84 years. In one group of thirty-two patients there were multiple and separate epidermoid carcinomata confined to the oral cavity. In the second group of sixteen patients there were malignancies of the oral mucosa as well as malignant tumors of the gastrointestinal tract. These lesions were studied microscopically, and the histories of the patients were evaluated.)

4. THE FATE OF HUMAN FOLLICULAR SACS IN HETEROLOGOUS TRANSPLANTATION. Martin Protzel.

(Human follicular sacs obtained from impacted teeth were transplanted to the anterior chambers of the eyes of guinea pigs. Growth and differentiation of the follicular implant were observed clinically and microscopically. Transplants took in 70 per cent and produced bone and cementum-like structures, but epithelial elements did not survive.)

5. HEMANGIOENDOTHELIOMA OF THE TONGUE. Irwin A. Small.

(In this case report, a tumor of the tongue of a newborn child was demonstrated and discussed.)

6. SYMPOSIUM—THE EFFECT OF HIGH-SPEED ROTARY DENTAL INSTRUMENTS ON THE PULP. Joseph L. Bernier (Moderator), Harold Stanley, Helmut Zander, and H. B. G. Robinson.

(The panel established that the pulp was a very sensitive organ with extensive reparative ability and that the reaction to operative procedures is the effect of transformation of energy and can be produced by any type of operative procedure. The effects produced are dependent on the method of use rather than upon rate of speed of the instrument. Just as much pulpal injury can be produced by conventional speed as by high-speed instruments, depending upon the method of use of the various instruments.)

7. The first annual Helen McClain Lecture was given by Lester R. Cahn. The title of the lecture was "The Oral Pathologist Looks at General Practice."

American Academy of Dental Medicine Announces Mid-Annual Meeting

The Academy's annual meeting will be held at the Hotel Sheraton-McAlpin in New York City on Sunday, Dec. 6, 1959. A business meeting for delegates and members will be held at 10 A.M., followed by a luncheon at 12:30 P.M.

A scientific program will be conducted from 2 to 5 P.M., featuring presentations on oral rehabilitation and the gingival tissue by essayists and clinicians well qualified in the field of dental medicine.

All members of the Academy and other interested dentists and physicians are welcome to attend. For program and reservations, address Dr. Andrew J. Cannistraci, 2152 Mulinen Ave., New York 62, New York.

American Association of Dental Editors

A business meeting will be held on Saturday morning, Sept. 12, 1959, at the Manhattan Hotel in New York City, beginning at 9 o'clock sharp. All members are urged to attend. The room number will be announced later.

Floyd D. Ostrander, President

University of Illinois

The Division of Postgraduate Education of the College of Dentistry will offer a concentrated two-week course in oral surgery, beginning Oct. 19, 1959.

The course will consist of lectures and demonstrations designed to cover all phases of exodontia and oral surgery, including applied pharmacology, anesthesiology, and radiology. It will include treatment of cysts, apicoectomy, mouth preparations for dentures, removal of impactions, and management of fractures.

Further information and applications can be obtained from the Division of Postgraduate Education, University of Illinois, College of Dentistry, 808 S. Wood St., Chicago 12, Illinois.

Loyola University

A research fellowship in prosthetic dentistry, beginning Sept. 1, 1959, is being offered by Loyola University School of Dentistry. This newly instituted research project deals with bone changes under removable prostheses and the problem of aging. The fellowship carries a stipend of $3,700.00 each year for one or two years. If desired, the Fellow may pursue a course of study leading to an advanced academic degree.

Requests for further information should be addressed to Dr. Arthur J. Krol, Chairman, Department of Prosthetic Dentistry, Loyola University School of Dentistry, 1757 W. Harrison St., Chicago 12, Illinois.

University of Minnesota

The third annual course in advanced oral pathology for 1960 will be given Thursday, April 21, through Tuesday, April 26, 1960. About half of the time will be devoted to examination of approximately 200 slides. Among the subjects and lecturers will be the following:

(1) Salivary Gland Pathology. Dr. John T. Godwin, Professor of Pathology, Emory University, Atlanta, Georgia.

(2) Bone Pathology. Dr. Louis Lichtenstein, Chief of Pathology, Veterans Administration Center, Los Angeles, California.

(3) Advanced Roentgenographic Diagnosis of Diseases of the Jaws. Dr. Edward Stafne, Professor Emeritus, Mayo Clinic, Rochester, Minnesota.

(4) Roentgenographic Technics for the Head and Neck. Dr. Richard W. Moss, Chief, Oral Surgery Section, Veterans Administration Center, Wood, Wisconsin.

(5) Dermatopathology. Dr. Robert Goltz, Professor of Dermatology, School of Medicine, University of Minnesota, Minneapolis, Minnesota.

(6) Odontogenic Tumors. Dr. Robert J. Gorlin, Professor of Oral Pathology, School of Dentistry, University of Minnesota, Minneapolis, Minnesota.

(7) Oral Manifestations of Systemic Disease. Dr. Anand Chaudhry, Professor of Oral Pathology, School of Dentistry, University of Minnesota, Minneapolis, Minnesota.

The course will be limited to twenty participants. Tuition will be $100.00.

Interested persons will please contact Dr. Robert J. Gorlin, Professor and Chairman, Division of Oral Pathology, School of Dentistry, University of Minnesota, Minneapolis 14, Minnesota.

New York University

The College of Dentistry, through its Department of Endodontia, will offer a forty-hour postgraduate course next winter on new developments in the treatment of vital and non-vital teeth.

Participants in the course will attend sessions from 9 A.M. to 1 P.M. on Wednesdays and Fridays. The lectures and demonstrations begin on Friday Feb. 26, and run through Wednesday, March 30, 1960.

The class will meet in the College's clinical building at 421 First Ave., in Manhattan. Instructing will be Dr. Morris B. Auerbach, chairman of the Department of Endodontia, and members of the department's postgraduate staff.

Further information can be obtained by writing to the Postgraduate Division, New York University College of Dentistry, 421 First Ave., New York 10, New York.

Ohio State University College of Dentistry

The 1959-1960 postgraduate courses in dentistry will be repeated according to the following schedule:

Complete Denture Prosthodontics. Dr. Carl O. Boucher. Oct. 12-16—May 9-13. Fee—$75.00.

General Anesthesia. Dr. Morgan L. Allison. Nov. 2-6—April 4-8. Fee—$75.00.

Oral Surgery. Dr. Morgan L. Allison. Nov. 9-13—April 11-15. Fee—$75.00.

Indirect Technics in Bridgework. Dr. Thomas F. McBride and Donald W. Dickson. Nov. 18-19. Fee—$25.00.

Bringing Operative Dentistry Up to Date. Drs. William Lefkowitz, Donald W. Dickson, and Harry H. Postle. Nov. 30—Dec. 4. Fee—$75.00.

Crown and Bridgework. Dr. Thomas F. McBride. Jan. 25-29. Fee—$75.00.

Pedodontics. Drs. Lyle S. Pettit and Benjamin H. Williams. Feb. 15-19. Fee —$75.00.

Endodontics. Dr. J. Henry Kaiser. March 1-4. Fee—$100.00.

Clinical Periodontics. Dr. John R. Wilson. April 11-15. Fee—$75.00

Partial Denture Prosthodontics. Dr. Victor L. Steffel. May 2-6. Fee—$75.00.

Dental Drugs in Action. Dr. W. Russell Kampfer. May 19-20. Fee—$25.00.

All the courses except "Indirect Technics in Bridgework" and "Dental Drugs in Action" will be given on five consecutive days, Monday through Friday.

Further information may be secured from the Postgraduate Division, College of Dentistry, 305 West Twelfth Ave., Ohio State University, Columbus 10, Ohio.

Temple University School of Dentistry

An intensive participation course in clinical endodontics will be offered under the direction of Drs. Leonard Parris and Herbert Schilder and their associates from 9 A.M. to 5 P.M. Oct. 26 through Oct. 31, 1959. Tuition will be $175.00.

The objective of this course is to train the dentist in clinical endodontic procedures. Sufficient material of a basic biologic nature will be presented to ensure a proper understanding and approach to the clinical phase.

The course will consist of lectures, supplemented by slides and clinical demonstrations. The postgraduate student will utilize diagnostic procedures, initiate treatment, and carry through to completion endodontic therapy on clinic patients. Single- and multirooted teeth will be treated.

Further information and application may be obtained by writing to Postgraduate Division, Temple University School of Dentistry, 3223 North Broad St., Philadelphia 40, Pennsylvania.

Tufts University School of Dental Medicine

A comprehensive demonstration course in complete denture construction (DPG. 701) will be given on the following Wednesdays: Oct. 28 and Nov. 4, 18, and 25, 1959. The course will be under the direction of Dr. Irving H. Hardy, professor of prosthetic dentistry (emeritus 1958). Tuition will be $125.00.

This course will deal with various aspects of complete denture construction, including diagnosis and treatment planning, evaluation of impression materials for individual cases, accurate determination of temporomandibular point relations and vertical dimension, selection and arrangement of teeth for optimum function and esthetics, using a central bearing mechanism as a guide, and instruction to the patient.

Further information may be obtained from the Director of Graduate and Postgraduate Studies, Tufts University School of Dental Medicine, 136 Harrison Ave., Boston, Massachusetts.

University of Alabama

The University of Alabama School of Dentistry will present five refresher courses during the month of October, 1959:

October 3 and 4. Oral Rehabilitation. Jerome M. Schweitzer.

October 10—12. Hypnosis Applied to Dentistry. William T. Heron.

October 17 and 18. Insurance, Investments, and Estate Planning. A. Key Foster.

October 24—26. Root Canal Therapy. Adeeb E. Thomas.

October 30 and 31, November 1. Crown and Bridge Prosthodontics With Emphasis on Pontic Construction and Fused Porcelain Veneers. John F. Johnston.

For further information, please contact the Director, Refresher Course Program, University of Alabama School of Dentistry, 1919 Seventh Ave., South, Birmingham, Alabama.

REVIEWS OF THE LITERATURE

BOOK REVIEWS

Oral Diagnosis. By Donald A. Kerr, D.D.S., M.S., Major M. Ash, Jr., D.D.S., M.S., and H. Dean Millard, D.D.S., M.S. St. Louis, 1959, The C. V. Mosby Company. 419 pages, 212 illustrations. Price, $10.00.

The three authors, faculty members at the University of Michigan School of Dentistry, have pooled their talents and teaching philosophies of the principles of oral diagnosis in this text. It is not a reference book of signs and symptoms of oral disease but, rather, a recording of the principles involved in obtaining and evaluating diagnostic information for orderly treatment. The foreword by L. M. S. Miner, written in 1937, states: "Not until diagnosis becomes the foundation on which the whole structure of dentistry is built can it lay claim to be a learned profession or an important branch of the great art and science of healing." Teachers and students of oral diagnosis will greatly appreciate the efforts of these three authors. If the principles as set forth are followed in dental practice, dentistry will more quickly achieve the aims expressed by Dr. Miner.

D. J. Holland.

The Management of Oral Disease. By Joseph L. Bernier, D.D.S., M.S., F.D.S., R.C.S. (Eng.). Second edition. St. Louis, 1959, The C. V. Mosby Company. 875 pages, 1031 illustrations. Price, $15.00.

The unusual opportunities provided by the Armed Forces Institute of Pathology have enabled the author to have access to undoubtedly the most complete collection of oral pathology material in the world. He has organized, condensed, and classified these data well. The oral diseases are discussed logically and consistently under headings of etiology, clinical features, histopathology, and treatment. The clinical photography and the reproductions of microscopic sections are superior. The references at the end of each chapter provide sources of additional detail and experiences wherever needed. *The Management of Oral Disease* by Bernier is a valuable addition to the list of texts on oral pathology and oral diagnosis.

D. J. Holland.

Treatment of Cancer and Allied Diseases. Volume 3. Tumors of the Head and Neck. By George T. Pack, M.D., F.A.C.S., and Irving M. Ariel, M.D., F.A.C.S. (editors). Second edition. New York and London, 1959, Paul B. Hoeber, Inc. 781 pages, 1028 illustrations. Price, $30.00.

Seventy authors have contributed to the most comprehensive and compact presentation of the essentials of treatment of neoplasm of the head and neck ever assembled in one volume. This is volume 3 in a set of nine separate and complete texts covering malignant disease of all systems and areas. The volume is divided into fifty-two chapters, each carefully compiled

by recognized authorities in special fields of oral, nose, pharynx, ear, and neck tumors. Both the so-called radical and conservative approaches—surgery and radiation—to malignancy in the head region are outlined. The most recent five-year survival rates and other statistical analyses clearly set forth the magnitude of the cancer problem. The illustrations, photographs, and diagrams are numerous and generally complement the text.

This volume is an excellent guide to practice as well as a convenient reference to any problem associated with malignant disease anywhere in the head and neck region.

D. J. Holland.